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CAUSALGIA FOLLOWING GUNSHOT INJURIES OF NERVES*†

Role of Emotional Stimuli and Surgical Cure through Interruption of Diencephalic Efferent Discharge by Sympathectomy

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"PERHAPS FEW PERSONS who are not physicians can realize the influence which long-continued and unendurable pain may have upon both body and mind. . . . Under such torments the temper changes, the most amiable grow irritable, the soldier becomes a coward, and the strongest man is scarcely less nervous than the most hysterical girl. . . . Nothing can better illustrate the extent to which these statements may be true than the cases of burning pain, or, as I prefer to term it, causalgia, the most terrible of all the tortures which a nerve wound may inflict." These comments were made by Weir Mitchell [25] in 1872, following an account originally written while he was seeing almost daily numbers of men suffering from gunshot wounds inflicted during the Civil War.

During the World War I not much progress was made in treating this condition, beyond the discovery that certain procedures were of little value. These included neurolysis, repeated resection of neuromata, proximal section of the affected nerve trunk or its chemical block, periarterial sympathectomy,** and division of the posterior spinal roots. In the major causalgias,[3] excluding rare and almost exceptional instances, all failed to give the hoped-for-relief. To make matters worse, the burning pain often persisted for years, so that

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**In addition to the earlier European reports, which have been summarized by Leriche,[38] Homans[14] and Fontaine and Herrmann[12] in this country have recorded a few successful results from this operation in the atypical minor causalgias, Südeck's atrophy, etc. Leriche, although advocating periarterial sympathectomy as a preliminary procedure, admits a considerable number of failures (4 out of 10). In cases of severe diffuse post-traumatic neuralgia, he has concluded that this operation is generally ineffective. A similar conclusion has recently been expressed by Ulmer and Mayfield,[39] in whose hands this operation was ineffective.

TABLE I.—*Summary of 13 Cases of Causalgia Treated by Preganglionic Sympathectomy.*

Case	Wound	Paralysis	Distribution of Pain	Time of Onset After Wounding	Hyperpathia	Trophic Changes	Temperature of Extremity	Sweating	Relation to: Cold, Emotion	Neurosurgical Procedures in Addition to Sympathectomy	Result of Sympathectomy on Causalgic Pain
1. Chas. R. Pfc. USMC	Small shell fragments L. upper arm.	Median nerve (partial)	Entire hand.	Few hours.	+++	+++	Cool.	+++	+++ +++	Early median neurolysis overseas, without improvement.	Complete relief, now plays strenuous games. Followed for 7 mos.
2. Chas. M Pfc. USMC	Rifle bullet through arm above elbow. Artery injured.	Median and ulnar nerves, complete at first, later spontaneous partial recovery.	Entire hand.	After operation for aneurysm.	++	+	Cold.	++	++ ++	Ligation of brachial artery 2 weeks after wounding.	Complete relief.* Followed 9 mos.
3. Norman C Pfc. USMC	Machine gun bullet passed between bones of upper forearm.	Median and radial nerves (partial).	Entire hand.	Few hours.	++	+++	Cool.	++	++ O	Previous neurolysis and partial suture of median and radial nerves with partial relief.	Complete relief. Followed 3 mos.
4. Fred S Pvt. USMC	Shell fragments upper arm and forearm.	Median nerve (partial), ulnar nerve (complete).	Entire hand.	5 hours.	+++	++	Cool.	+++	+++ +++	Subsequent median neurolysis and ulnar nerve suture.	All hyperpathia cleared.* Followed 1 year.
5. John H Maj. USMC	Upper humerus fractured by shell fragment. False aneurysm in axilla.	Median nerve (complete), ulnar nerve (partial).	Entire hand, but most marked in ulnar area.	Immediate.	++	+	Cold.	++	++ +++	Ligation of axillary artery. Median nerve sutured later.	Complete relief. Followed 1 year.
6. Robt. B Cpl. USMC	Bullet wound brachial plexus, fractured clavicle, severed subclavian artery.	Median (complete), ulnar nerve (partial), musculocutaneous and medial antebrachial cutaneous nerves (complete).	Entire hand, most severe in ulnar area.	1 week.	+++	++	Cool.	O	++ +++	None.	Complete relief. Followed 8 mos.

* See footnote on next page.

TABLE I (*Continued*)

Case	Wound	Paralysis	Distribution of Pain	Time of Onset	Hyperpathia	Trophic Changes	Temperature of	Sweating	Relation to: Cold, Emotion	Neurosurgical Procedures	Result of Sympathectomy

TABLE I (*Continued*)

Case	Wound	Paralysis	Distribution of Pain	Time of Onset After Wounding	Hyperpathia	Trophic Changes	Temperature of Extremity	Sweating	Relation to: Cold, Emotion	Neurosurgical Procedures in Addition to Sympathectomy	Result of Sympathectomy on Causalgic Pain
7. Nathan V. Pvt. USMC	Rifle bullet through upper forearm with fracture of ulna.	Median nerve (partial).	Median distribution.		++	+++ (median area).	Cold.	++	+ ++	Neurolysis median nerve without relief.	Complete relief. Followed 5 mos.
8. Harold O'S. Pfc. USMC	Shell fragment wound of internal condyle of elbow.	Ulnar nerve (partial).	Ulnar area of hand.	Immediate.	++	+	Cold.	+++	++ ++	Previous ulnar neurolysis without benefit.	Complete relief. Followed 5 mos.
9. Howard W. Pfc. USMC	Bullet wound below elbow.	Median nerve (partial).	Median area of hand.	Immediate.	++	+	Cold.	+++	++ ++	Previous median neurolysis without improvement.	Complete relief. Followed 5 weeks.
10. Alfred D. Pfc. USMC	Mortar wound median side of shoulder, axilla to mid arm.	Median nerve (partial), musculocutaneous (complete).	Median area of hand.	Day after wound.	+++	+	Cool.	+	++ ++ **	Block of brachial plexus without relief.	Complete relief. Followed 13 mos.
11. Wm. M. Cpl. USMC	Phosphorus grenade fragments in lower leg.	Posterior tibial and common peroneal (partial), sural nerve (complete).	Entire foot and toes.	Immediate.	+++	++	Cold.	++	++ ++ ***	None.	Incomplete sympathectomy failed to relieve pain in anterior third of foot. Satisfactory improvement following completion of sympathetic denervation and neurolysis. Follow-up period of 12 months.*
12. John B. GM 2/c	Razor slash across palm.	Median nerve paralysis at first complete, then partial recovery.	Median area.	6 months after wound with nerve recovery.	++	+	Cold.	++	+ ++	Immediate median nerve suture.	Satisfactory relief.* Followed 3 mos.
13. John McC. Lt. (jg) USNR	Penetrating wound of lower thigh.	Posterior tibial (partial), and common peroneal nerves.	Sole of foot, especially on medial side.	Immediate.	+++	+	Cool.	+	++ +++	None.	Complete relief. Followed 2 mos.

* Residual paresthesia and hyperesthesia of a different type connected with recovery of the injured sensory axones (see discussion).

** Patient 10 had such severe exacerbations of pain in his hand on swallowing anything cold that he was only able to sip warm liquids. This most unusual complaint was relieved immediately following procaine block and disappeared permanently after preganglionic sympathectomy.

*** Patient 11 complained of increase in his pain on urination and defecation, a feature which has previously been commented upon. This complication has been relieved by sympathectomy.

when John Mitchell reviewed the subsequent history of some of his father's cases in 1895 he found a considerable number who had continued to suffer permanently. Leriche[18] also has recorded a case of 17 years' duration. In a few cases the burning pain undoubtedly subsides with time and spontaneous or surgical repair of the injured nerve, but the interval is often so long that irreparable changes have taken place in the skin, muscles, bones, and, most serious of all, in the individual's psychic constitution. As a result drug addiction, deterioration of the personality, and ultimate suicide have been frequent terminal results.

In the 1920's progress in therapy began with the discovery of effective methods of sympathetic denervation of the limbs. The work of Leriche in Strasbourg, which is best summarized in his book on "The Surgery of Pain,"[18] was a great stimulus, and it is to him, more than to any other, that credit is due for pointing out the role of the sympathetic nervous system in the causalgic syndrome. Sporadic favourable results of surgical interventions on the sympathetic ganglia were also published by Spurling,[35] Ross,[32] Kwan,[17] Livingston,[20] and others. During World War II rapid strides were made, especially by British and American surgeons. It has now become apparent that the classical syndrome of major causalgia, with related emotional and autonomic manifestations, can be treated by early sympathetic denervation of the arm or leg with consistent success. Case reports to back up this statement have been published by Doupe, Cullen, and Chance,[9] Mayfield and Devine,[22] Speigel and Milowsky,[34] Rasmussen and Freedman,[28] Tyson and Gaynor,[38] Albritten and Maltby,[2] and Ulmer and Mayfield.[39] The following series of 13 cases gives added confirmation and emphasizes the role played by the sympathetic nervous system.

CLINICAL PICTURE OF CAUSALGIA

The clinical picture of major causalgia with burning pain in the hand or foot, trophic changes in the skin, subcutaneous and bony structures, and autonomic stigmata of excessive vasomotor and sudomotor activity is so well known (Leriche,[18] Livingston,[20] de Takáts[36]) that it will not be discussed here. As Livingston has pointed out, it is unfortunate that so many observers, including Mitchell himself, have included so many conditions with burning pain as the only point in common under the diagnosis of causalgia. Other conditions causing persistent pain and hyperesthesia after nerve wounds have recently been discussed by White;[41] Südeck's atrophy, so-called reflex dystrophy, post-traumatic arthritis, and neuralgia in amputation stumps should be definitely excluded from this classification. In our opinion the term causalgia should be limited to include only the sequelae to penetrating wounds of the extremities, which cause injury to the nerve trunks and the triad of burning pain, trophic changes, and autonomic phenomena. This is such a distinct clinical entity that there should be no difficulty with its differential diagnosis.

As regards the vasomotor changes, some observers, notably Mitchell[25] and de Takáts,[36] have been struck by the tendency to local warmth and

vasodilatation,* but this phenomena is certainly not a constant one. Livingston[20] has taken exception to this view, as he found relatively few instances where a local rise in temperature was a persistent feature. More often, when it does occur, it is transient and is followed by a fall in temperature so that the involved part becomes colder than normal. In Ulmer and Mayfield's[39] series they found 35 patients with cold and 40 with hot extremities, whereas in our group all 13 patients had cold and moist extremities (see Table I). Perhaps the difference may arise in the date at which these individuals are first examined. Mitchell must have seen his Civil War wounded and de Takáts his civilian patients at an early date, whereas our sailors and marines evacuated from distant outposts in the Pacific required longer time to reach the hospital than the European wounded treated by Mayfield and his associates. While de Takáts[36] has shown by oscillometric tracings that the vasodilator response is unilateral, the vasoconstriction and abnormal sweating which we have observed usually involve the other extremities as well, although often to a lesser degree. It is quite possible that cutaneous vasodilatation is the characteristic condition in the early phase of causalgia, but after a time at least the opposite is most frequently the case. Everyone who has studied the condition in the recent war wounded has been impressed by the profuse sweating of the involved hand or foot, but nervous sweating of the palms and soles is a common phenomenon in wounded men, especially when pain or worry are prominent features.

The principal purpose of this paper is to emphasize the importance of thermal and emotional factors on aggravation of pain, and the effectiveness of sympathectomy in its relief. In order to bring out the salient factors on which the etiology of the condition depends and the rationale of eliminating the efferent sympathetic discharge to the painful limb, we plan to present our clinical data first and to discuss their implications afterwards. For convenience, the most important features of each case are summarized in Table I and further details are given in the brief case histories of each of the 13 patients which follow.

CASE HISTORIES

Case 1.—Charles R., 21 years, Pfc., U.S.M.C.: On Okinawa on 5/1/45 this private received multiple wounds from a "booby trap" in the head, right thigh, and left upper arm. Within a few hours he noticed the onset of burning pain in the left hand, together with a sense of partial numbness in the second and third fingers. All his wounds healed uneventfully. On 6/18/45 at another hosptial the median nerve was explored and minor adhesions freed, without the least benefit. On admission to the U. S. Naval Hospital at St. Albans on 7/16/45 he complained of constant diffuse burning pain in the entire hand and lower forearm, which was increased by cold, sudden noises, and any form of apprehension. He could not tolerate the minor disturbances on the open ward, and he kept his hand constantly moist with a wet towel or by immersion in a basin of lukewarm water (Fig. 1A.)

* In a previous article one of us[41] attempted to explain pain during states of vasodilation, as well as during constriction, to the overactivity of sympathetic vasodilator fibers. Such fibers have been postulated on the basis of observations made by Lewis and Pickering,[19] but the recent work of Sarnoff and Arrowood[33] has made this hypothesis untenable.

FIG. 1A.—*Case* 1. Preoperative photograph of patient guarding painful left hand and soaking it in lukewarm water.

FIG. 1B.—Postoperative photograph showing free use of formerly sensitive hand.

He was suffering so much that he begged for early relief. Accordingly diagnostic paravertebral procaine block was performed on the day after his admission. The nervous apprehension caused by this procedure resulted in such severe throbbing pain that it was necessary for a hospital corpsman to drip lukewarm water over the lower arm and hand while the needles were being inserted in his back. However, within a minute of the time the infiltration of procaine began the discomfort disappeared, and a few minutes later the cold extremity became warm and dry. That evening he went to the movies for the first time, but noticed some recurrence of his pain. Left thoracic preganglionic sympathectomy was performed two days later, followed by complete relief. He got up on the first postoperative day and was able to move out on the open ward and use his hand without discomfort (Fig. 13.) Shortly thereafter he began to play volley ball and other strenuous games, and was then discharged from the Marine Corps to enter civilian work.

Case 2.—Charles M., 19 years, Pfc., U.S.M.C. On 2/28/45 at Iwo Jima this marine was struck by a bullet in the right upper arm and flank. The bullet, which traversed the lower third of his arm, caused a partial injury of the median and ulnar nerves, nicking

the brachial artery as well. Eleven days later the resulting aneurysm was operated upon at Pearl Harbor. Immediately afterward he began to complain of burning pain deep in the hand, made worse by cold, touching the extremity, or by excitement such as that caused by watching a baseball game or by a close call in an automobile. On arrival at St. Albans he had a cold hand without any radial pulse, the characteristic signs of median and ulnar paralysis, and severe ischemic fibrosis of the flexor muscles in his forearm. On 8/21/45, a week after his admission, following temporary relief obtained by paravertebral procaine block, his moderately severe causalgia was relieved by preganglionic sympathectomy. Although the relief of his burning pain and hyperesthesia was complete and the hand became totally dry, there was little increase in temperature in the anesthetic median and ulnar areas (see below under discussion). Since this operation he has been hospitalized for a period of six months for plastic procedure to release scar tissue contractures in his forearm and elbow. No operation on the injured nerves has been necessary because of their spontaneous regeneration. We have been interested to observe that with early return of sensation he has developed the usual mild cutaneous hyperesthesia that accompanies nerve regeneration, but without any trace of his previous burning pain. This has been a common finding in other cases.

Case 3.—Norman C., 23 years, Pfc., U.S.M.C.: A machine-gun bullet passed through the left forearm on 1/5/45, causing partial paralysis of the median and radial nerves. Five hours later, on recovering from anesthesia for débridement of the wound, he began to suffer from causalgic pain through his hand. Neurolysis and partial suture of both partially paralyzed nerves had been performed four months prior to his admission to St. Albans, and this had resulted in some improvement in his burning pain, but he still complained of severe stabbing, shooting pain in his wrist and hand. This was made definitely worse by cold weather but was not related to emotion. We regarded this as a somewhat atypical case of causalgia, but we obtained satisfactory relief by diagnostic procaine block. Preganglionic sympathectomy, performed on 9/5/45, has been followed by a complete remission of all his complaints. During the three months that have elapsed since operation there has been only partial vasodilation in the residual hypesthetic territory of the median nerve (see below under discussion).

Case 4.—Frederick S., 19 years, Pfc., U.S.M.C.: Multiple wounds in the right upper and lower arm were received at Okinawa on 5/10/45 (Fig. 2) with partial median and complete ulnar paralysis. His burning pain began five hours after he was wounded. Next to Case 1, this patient had the most severe causalgia of the entire series. When he was admitted to St. Albans in July the burning pain involved his entire hand. This became much worse in the cold and quite unbearable on any psychic disturbance, so that he lay in a quiet, darkened room with his arm immobile on the bed (Fig. 2A) and usually protected by moist towels. He complained particularly of the aggravating effect of loud noises, jarring of the bed, exciting movies or any other psychic stimuli, of cold draughts of air over his hand or cold, rainy weather. The patient stated that each night when he got quieted down and relaxed his pain largely disappeared and he was able to sleep well, but it would appear again soon after he awakened. At the time of his admission he unfortunately had a complicating infectious hepatitis, so that we did not dare submit him to general anesthesia and operation until his jaundice cleared. During this period of waiting his causalgia was relieved three times by paravertebral procaine infiltration of the upper thoracic ganglia, only to recur within a few hours on each occasion. Finally sympathectomy was performed on 9/19/45 and his causalgia disappeared from this date.

A week later the nerves in his arm were widely exposed and a long gap in the ulnar repaired by transplantation and suture. Figure 2B shows the complete injury to the ulnar nerve and the surrounding adhesions of the median, which undoubtedly gave rise to the causalgic syndrome. In the forearm there were only fine adhesions to each trunk. Following suture the patient made excellent progress in nerve regeneration at the rate of

FIG. 2A.—*Case* 4. Preoperative photograph of patient to illustrate wounds in arm and characteristic position in which patient kept it immobilized. Hand was usually protected by moist towel. Note moisture of palm and trophic changes.

3.5 mm. per day. It is again of interest to note that, whereas vasodilation of the median area was complete following preganglionic sympathectomy (skin temperature of the first three fingers in a room at 67° being between 86.5° and 90°), the temperature in the hemianesthetic ring finger measured 90° on the median and 86° on the ulnar side, and in the completely denervated little finger, where there was complete degeneration of the post-

ganglionic sympathetic fibers, was reduced to 74°. (See discussion below. He has been under observation for one year and remains free of his former burning pain.

Case 5.—John H., 25 years, Maj., U.S.M.C.: This officer was struck by shell fragments at Okinawa at 5/4/45, from which he sustained a compound fracture of the surgical neck of the left humerus and other injuries of lesser importance. The missile, which entered his axilla, partially divided the axillary artery and ulnar nerve, and severed the median. Severe causalgic pain developed immediately throughout his entire hand. On admission to St. Albans he was in poor general condition and still had an unhealed wound in his left axilla. This soon began to extrude clots of blood so that it was necessary to ligate the axillary artery on 9/15/45 to prevent serious hemorrhage. This operation permitted evaluation of the nerve injury, but median suture in the presence of sepsis was out of the question. It was of interest that this patient, in addition to noticing an increase

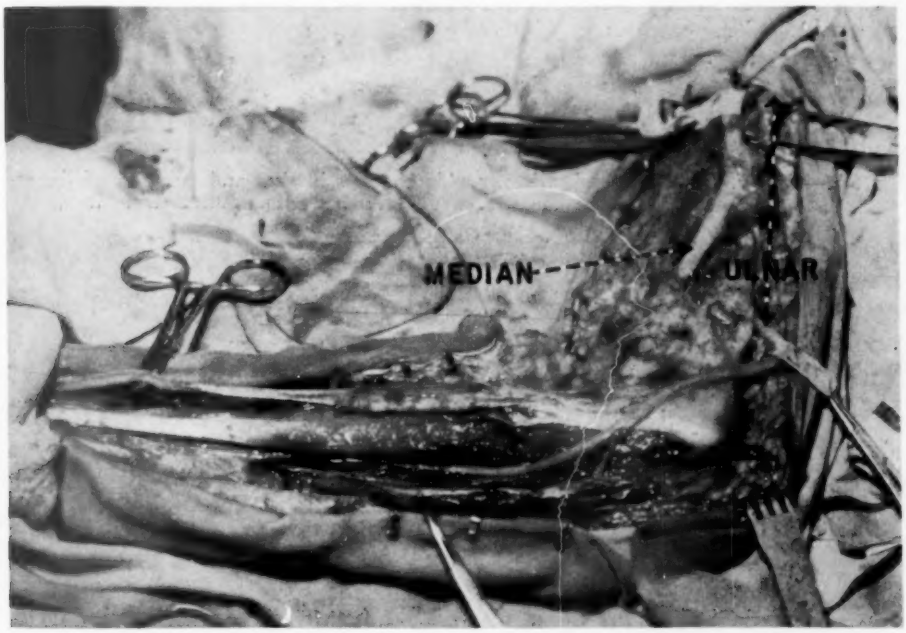

FIG. 2B.—Photograph taken at secondary exploration preliminary to suture of severed ulnar nerve. Note wide gap in ulnar and lateral neuroma of median nerve In lower forearm neither median nor ulnar nerves were injured. The median is shown elevated by the hemostat.

in his burning pain on cold and psychic stimuli, complained bitterly of the throbbing pain in his hand during any slight argument or whenever his children cried. Following diagnostic block, thoracic sympathectomy was performed on 9/27/45 and has produced an excellent result to date (12 months). His median nerve was sutured on 3/6/46, a month after final healing of his wound. In this patient, as in Cases 2, 3, and 4, there was no vasodilatation in the cutaneous area of the median nerve, where the postganglionic sympathetic fibers had degenerated from the injury to the nerve trunk (skin temperature of first three fingers averaging 72°, but 90° in fifth finger). The physiologic reasons for this phenomenon are given below (see discussion). He remains free of pain at the end of a year.

Case 6.—Robert B., 23 years, Cpl., U.S.M.C.: On 6/19/45 this patient had received gunshot wounds resulting in compound fractures of the left clavicle and right femur.

There was an accompanying partial paralysis of the brachial plexus and injury to the subclavian artery. Emergency treatment consisted of débridement without direct exposure of the nerves. His causalgic pain developed a week after his injury. On admission to St. Albans he complained of constant hyperpathia with intense throbbing on exposure

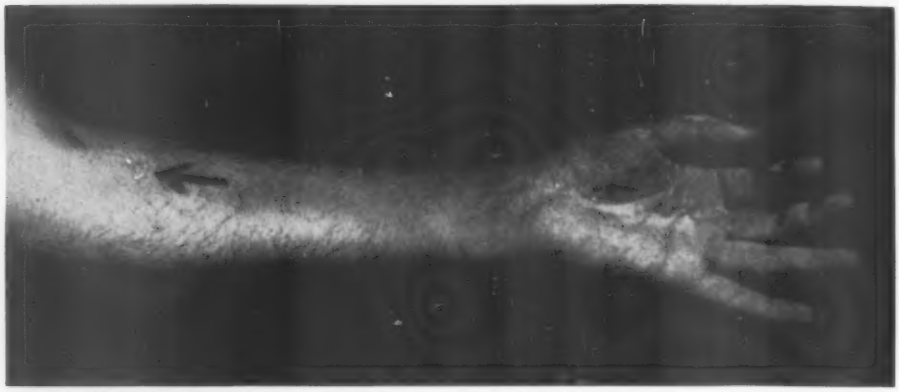

FIG 3A.—*Case 7.* Photograph showing trophic changes in skin and tapering of fingers in area innervated by median nerve. The arrow points to bullet wound.

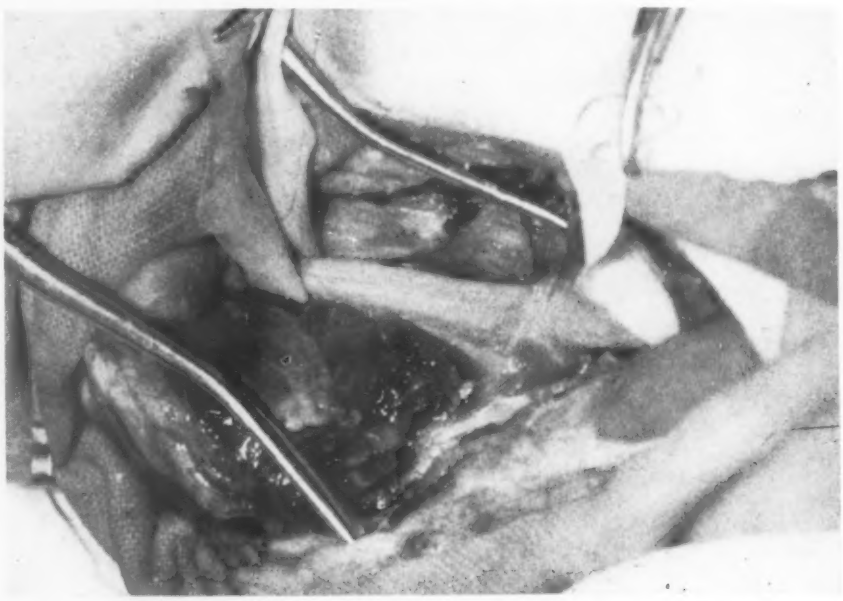

FIG. 3B—Appearance of median nerve at preliminary exploration. Note filmy cicatricial adhesions.
(This figure is reproduced with the permission of the *American Journal of Surgery,* where it was first published by White[11].)

to cold and psychic stimuli (loud noises, vibrations, annoyance, or excitement). There was paralysis of the musculocutaneous and median nerves, the ulnar being less extensively involved. The causalgic pain, as is so commonly the case, was in the area of the incompletely paralyzed ulnar nerve. After successful procaine block, an upper thoracic preganglionic sympathectomy was performed on 9/27/45, which has resulted in com-

plete relief of his causalgic pain. At the end of eight months there has been good spontaneous recovery of both nerves, with fair return of function in the proximal group of muscles controlled by the median.

Case 7.—Nathan V., 28 years, Pfc., U.S.M.C.: A rifle bullet through the left elbow at Iwo Jima on 3/4/45 caused a slight injury of the median nerve. In this patient the area of burning pain, cutaneous trophic changes, and tapering fingers were limited to the territory of the injured nerve (Fig. 3A). For this reason a neurolysis of this nerve was performed first (Fig. 3B), but without any relief. Diagnostic procaine block and subsequent thoracic sympathectomy gave most satisfactory results.

Case 8.—Harold O'S., 22 years, Pfc., U.S.M.C.: On 3/11/45 a shell fragment caused a partial injury of the right ulnar nerve at the internal condyle. The patient began to notice causalgic pain as soon as he recovered from an accompanying cerebral concussion. When he was admitted to St. Albans he suffered from moderately severe burning pain and hyperesthesia in the ulnar area of his hand, aggravated by cold and the usual psychic factors. The first attempt to block his upper thoracic sympathetic ganglia resulted in vasodilatation, but failed to produce satisfactory drying of the skin or any Horner's sign; furthermore, his pain was not relieved. Following a second, effective diagnostic block and throughout the five months he was under observation following surgical preganglionic denervation he remained free of pain.

Case 9.—Howard W., 30 years, Pfc., U.S.M.C.: This patient received a through-and-through bullet wound between the two bones of the right upper forearm on 9/21/44 at Peleliu. With the partial injury of his median nerve he noticed immediate onset of causalgia limited to the area supplied by this nerve. On 3/26/45 the nerve was explored and freed of adhesions, but without significant effect on his pain, which remained fairly troublesome eleven months after the receipt of his wound. Following a diagnostic chemical block, a preganglionic sympathectomy was carried out on 19/29/45. This has produced very successful warming of his cold hand and effective relief of his pain.

Case 10.—Alfred D., 22 years, Pvt., U.S.M.C.: This man was injured by fragments of mortar shell explosion in the upper arm on 9/16/44 at Peleliu. There was complete paralysis of the musculocutaneous and partial of the median nerve. Severe causalgic pain appeared in the area of its palmar distribution the day after he was wounded. He described this pain as intense burning and throbbing in the thenar side of his hand, which was increased by any light touch or rub, or by any sudden noise, mental upset, fright, anger, or excitement. Instead of being aggravated by cold, this patient complained particularly of hot weather, when he had to protect his hand by ice or cold, wet packs. The most striking feature of all was the relation of his pain to any attempt to swallow cold liquids. This began a month after his wounding and forced him to limit his fluid intake to sips of warm milk. Brachial plexus block with procaine at another hospital had failed to relieve his pain, but the result from paravertebral infiltration of the sympathetic ganglia in our hands was excellent. For the first time he was able to drink a tumbler of cold water. Preganglionic thoracic sympathectomy, performed on 11/14/45, gave a most satisfactory result. At the end of thirteen months he has no further complaints and is very happy to be able to drink cold liquids, especially beer. In spite of residual biceps paralysis, he has good use of his arm, which has now recovered normal sensation in the hand and a fair degree of elbow flexion through compensatory ("trick") movement by the brachioradialis muscle.

Case 11.—William M., 20 years, Cpl., U.S.M.C.: This Marine Corps corporal was struck on 5/5/45 by a phosphorus grenade, which resulted in multiple wounds of the knee and lower leg with complete paralysis of his sural and a partial injury of his right peroneal and posterior tibial nerves. Immediately afterwards he noticed extremely disagreeable burning pain throughout his foot, except in the anesthetic area on its lateral aspect. At the time of his admission the burning pain and hyperesthesia were intense and were greatly augmented by cold or psychic factors. In addition, his knee

was ankylosed in extension and his foot contracted in a severe equinus position. The sole of his foot and toes were deeply incrusted in brownish desquamating skin, which could not be washed off on account of the pain. His pain was also increased during urination and defecation. The patient was unable to walk or to think of anything beyond his painful condition. We felt so certain that sympathectomy would bring about adequate relief that the operation was done on 11/26/45 without preliminary injection of procaine. In this operation through the retroperitoneal approach two well defined ganglia and 2.5 cm. of the lumbar chain were removed below the crus of the diaphragm.

Although the immediate result was encouraging, the patient began to complain of recurrent burning pain and hyperesthesia in his toes and the ball of his foot on the third day. The result in the posterior two-thirds of his foot remained satisfactory, but the anterior third soon became as painful as ever. On careful inspection, however, it was evident that there were tiny drops of sweat on the toes. Residual sudomotor activity was confirmed by Victor Minor's starch-iodine test[23] (Fig. 4) and by the low cutaneous resistance to a galvanic current demonstrated by Richter's Dermometer.[31] On examination of the postoperative lumbar roentgenogram it was found that the lowest metallic marker clip was at the level of the upper portion of the third lumbar vertebra. It therefore seemed probable that the cause for the residual pain in the distal portion of this patient's foot was due to the presence of an undivided white ramus communicans connecting the spinal cord with the paravertebral sympathetic chain at an abnormally low level. This possibility was put to the test by paravertebral injection of procaine against the side of the fourth lumbar vertebra on two occasions, with complete disappearance of the persistent hyperpathia in the toes. On 1/4/46 the anterolateral surface of the third and fourth lumbar vertebrae was widely exposed through a midline abdominal incision with separation of the posterior peritoneum to the right of the vena cava and common iliac vessels. Another 3 cm. of sympathetic trunk was removed, including a large ganglion situated a centimeter above the point where the trunk disappeared beneath the iliac vessels. Two months after this added resection of the lower lumbar chain the patient was distinctly improved. It was then possible to manipulate all his toes, which were formerly too sensitive to permit washing the skin or cutting the nails. Trophic changes in the skin cleared. The buring pain on cold and psychic stimulation also disappeared. At 12 months, after added neurolysis of the injured nerves, he is free of pain and receiving orthopedic rehabilitation for his stiff knee and the contraction deformity in his foot.

FIG. 4.—*Case* 11, after preliminary incomplete sympathectomy. Areas of residual sweating demonstrated by Victor Minor's starch-iodine test and outlined by dotted lines. The dark area in the toes and anterior foot corresponded exactly with the patient's residual hyperpathia.

Case 12.—John B., 19 years, GM 2/c, USN: An injury of the median nerve in the palm of his right hand was caused by a razor slash received on 6/2/45. Suture of the severed median nerve at the base of the palm was performed an hour later and the incision healed well. During the period of complete paralysis the patient experienced no pain. At the end of six months, however, with partial reinnervation of the palmar and digital median branches, severe burning and hyperesthesia developed in this portion of the hand. These sensations became much worse on exposure to cold or emotional

excitement, and he noticed them particularly when he went to exciting movies or to a shooting gallery. At these times sweating was also greatly increased in the ulnar area of his right hand, and in the left also, though to a lesser extent. Following thoracic preganglionic sympathectomy on 2/6/46 all the intense burning pain has disappeared. Cold and excitement no longer induce disagreeable throbbing and burning. With partial sensory recovery to the base of the first three and a half fingers the sense of paresthesia and less intense hyperesthesia, which characteristically accompany nerve recovery, are still a source of mild complaint. These residual sensations, however, in no way resemble his former incapacitating causalgic pain. Two weeks after his sympathectomy the median nerve was re-explored and freed of scar tissue. With its gradual regeneration and the redisposition of myelin around the sensory axones the quality of sensation should return to normal.

Case 13.—John McC., 28 years, Lt. (j.g.) U.S.N.R.: On 3/27/45, while flying over Iwo Jima, this pilot was struck by a fragment of flak which passed transversely through the posterior portion of his left thigh at the level of the hamstring tendons. There followed immediate foot drop and aching, burning pain in the sole of his left foot. This became difficult to bear before he was able to land his plane. There was no injury to the popliteal artery and his wound healed without infection. During the next 12 months, prior to his admission on the neurologic service, his causalgia was a constant source of severe pain and total incapacity. It was made much worse by all the usual cold and psychic stimuli, and also whenever he laughed. He found that he was more comfortable when he wore a thick wet sock or one impregnated with vaseline. At times, when the pain became particularly severe, he would immerse his foot in a bucket of cool water. When put in a room next to the galley, the noises were so troublesome that he had to be moved. He obtained more relief from a stiff drink of whiskey than from an injection of morphine.

On examination a year after his injury it was found that there was considerable spontaneous recovery of the peroneal and a residual partial damage to the posterior tibial nerve. The burning hyperesthesia involved the sole of his foot, especially in the area of the medial plantar nerve.

Paravertebral lumbar procaine block was followed by complete temporary relief and a restoration of normal sensation. Following lumbar sympathetic ganglionectomy on 3/22/46, he was up on the fourth day and has been fully relieved of his pain (2 months observation).

DISCUSSION

In giving our clinical data first we have purposely not adhered to the usual order of a medical paper, because the findings recorded in Table I and the individual case histories have so much bearing on the etiology of causalgia and its surgical treatment, which we intend to discuss in the light of the clinical observations presented above.

INCIDENCE

No statistics are available as to the rate of incidence of causalgia in previous wars, but in the present conflict Ulmer and Mayfield[39] have reported 75 cases amongst 1477 peripheral nerve injuries at the Percy Jones General Hospital; Speigel and Milowsky[34], seven cases in 275 soldiers at another U. S. Army Hospital; and we have seen this complication 13 times in some 400 sailors and marines with wounds of the peripheral nerves at the U. S. Naval Hospital in St. Albans. This represents a rate of incidence after penetrating wounds of nerves in the range of 2.0 to 5 per cent.

ETIOLOGY

Many aspects of the causalgic syndrome suggest that it is a form of psychoneurosis, and this diagnosis has often and most unfairly been applied to these victims. The fact that the whole pseudo-neurotic picture so often clears immediately following suitable surgical intervention, when the sufferer has lost his dread of pain, no longer requires sedatives, and can resume a normal life, indicates that the personality disturbance is a result rather than the cause of an unendurable condition. This is well illustrated by our first patient. Prior to his sympathectomy he had become a neurotic recluse and remained almost motionless in a quiet room with his arm protected by a moist towel. He was so preoccupied with his painful hand that he was able to think of nothing else. Immediately after operation, however, he joined the other men on the open ward, became carefree and gay, and was soon able to take part in strenuous games. In the past, when no successful treatment was known, causalgia was a frequent cause of drug addiction and often led either to deterioration into hopeless invalidism or to self destruction. Psychologic studies made on service personnel after successful treatment in the recent war (Mayfield and Devine;[22] Speigel and Milowsky[34]) and in civilians (de Takáts[36]) have not brought to light any predisposing psychogenic factors.

In reading through Mitchell's fascinating monograph on "Injuries of Nerves" and also the earlier account of Mitchell, Morehouse and Keen[26] one gains the impression that causalgia was much more common in the War between the States than in either the first or second World Wars. On first thought it would seem likely that this is due to the decreasing rate of wound sepsis. Mitchell pointed out that "every possible precaution should be taken to lessen the chance of deep inflammation and the secretion of pus." Certainly there has been a far lower incidence of sepsis in the gunshot wounds of the recent war, but nevertheless we have seen severe causalgia in several patients where the wound healed per primam. Furthermore, the usual early onset of causalgic pain is strong evidence against the etiologic importance of sepsis. One of the most impressive features about our cases was the rapidity with which burning pain developed after the wound. In all but two of the 13 patients in whom the exact time of onset is recorded it began during the first day, and most of the men noticed it either at once or within the first few hours. Leriche[18] and Ulmer and Mayfield[39] have also noticed the frequent, almost immediate onset of causalgia. This eliminates not only sepsis but also ascending neuritis (so frequently mentioned in older accounts), anoxia due to fibrosis, and compression of the nerve by scar tissue or neuroma formation. There have been occasional reports indicating that at times the pain may be caused by the proximity of a foreign body, but we have recently removed a considerable part of the movement of a wrist-watch from a Marine Corps officer's median nerve where there was no history of pain at any time. Livingston,[21] however, has described the relief of median nerve causalgia in a Marine private wounded at Guadalcanal following the removal

of a shell fragment from the upper arm. In this case movement of the metallic fragment produced shocks along the course of the nerve. Under such circumstances it is logical to remove the foreign body, but neurolysis with freeing of adhesions and transplantation of the nerve into a healthier tissue bed has rarely influenced the pain (see Cases 1, 3, 7, 8, 9 and Fig. 3B).

In addition to the factors listed above, injury to a major blood vessel has been cited as a possible cause of burning pain. Leriche[18] reports relief of pain following excision of the traumatized sections of arterial trunks, but in our cases only three out of 13 patients had coexistent arterial injuries. None of Ulmer and Mayfield's[39] large series are reported as having associated wounds of major arteries.

Our cases summarized in Table I and the recent reports of other neurosurgeons in the American and British Armies[2, 10, 22, 28, 34, 38] have shown the effectiveness of sympathectomy in the relief of causalgic pain. Case 11, in whom the first incomplete lumbar sympathetic ganglionectomy gave only partial relief, lost the burning hyperpathia in his toes after remaining lower sympathetic connections were interrupted. The effectiveness of sympathectomy casts an interesting light on the etiology of causalgia. In spite of the belief held by some writers, notably Kuntz and Saccomanno,[14] that sensory fibers reach the spinal cord along the sympathetic nerves, the great majority of the anatomic, physiologic, and clinical evidence is against this.* Kuntz's experiments were performed on cats and it is not certain that section of the spinal cord between the second and third lumbar spinal segments would eliminate all somatic efferent connections from the lower extremity, especially on stimulation of the femoral nerve or application of a tourniquet above the knee. Furthermore, why should reduction of the stream of efferent sympathetic motor impulses which occurs in a quiet environment, after the ingestion of alcohol, in sleep, and during bouts of fever reduce causalgic pain? These individuals soon learn that they are most comfortable in a warm, quiet room and must avoid psychic stimulation of any sort. We were at first much surprised by the increased comfort of our patients during the quiet hours of the night, when sleep greatly reduces the activity of the sympathetic centers in the hypothalamus. Mitchell commented on this also, stating that "it is quite rare for a patient to arouse from sleep with pain, and I have heard men remark that it took some time to get awake to the pain." Patient 13 of our series stated that a moderate amount of alcohol gave him more comfort than an injection of morphine. Fever induced by intravenous foreign protein and by general heating of the body also reduces efferent vasoconstrictor tone. Mayfield and Devine[22] have observed several striking remissions of causalgic pain after periods of malarial chill, which should have no effect on pain

* Since this manuscript was submitted, one of us (J.C.W.) has stimulated the second and third lumbar ganglic in the course of resection of the sympathetic chain under local anesthesia. The patient, an intelligent observer suffering from pain in a thigh amputation stump, reported ipsilateral low abdominal and pelvic pain, but no reference whatsoever to his leg.

transmission but would result in reduction of vasoconstrictor discharges from the hypothalamus. This is also true of the new drug tetraethylammonium bromide, the pharmacologic action of which has recently been investigated by Acheson and Moe.[1] From a recent clinical study by Berry, Campbell, Lyons, Moe, and Sutler[5] and in further unpublished reports by Campbell,[8] it is clear that this compound, which blocks the synapse between the sympathetic pre- and post-ganglionic neurones, but has no effect on sensory fibers, will effectively stop the burning pain of typical causalgia following nerve injury. On the other hand, causalgic pain is aggravated by any increase in these tonic impulses, such as occurs in cold, damp, or very hot weather, or during psychic irritation. Quoting again from Mitchell's account: "The constitutional condition, reacting on the wounded limb, exasperates the hyperesthetic state, so that the rattling of a newspaper, a breath of air, the step of another across the ward, the vibrations caused by a military band, or the shock of feet in walking, gives rise to increase of pain."

It is our contention that the "hyperesthetic state" is both caused and aggravated by autonomic impulses, released at the hypothalmic level in response to thermal and psychic stimuli, and distributed over efferent sympathetic neurones.

We have recently requested our patients to write down the irritative environmental factors which convert the ever-present sensation of burning pain and hyperesthesia into a state of throbbing torture. The list includes the following interesting statements:

Cold, damp or very hot weather.

Cold air on the hand.

Loud or unexpected noises, annoying radio programs.

Jarring of the bed.

Anything exciting such as a narrow escape, a harrowing movie, stirring music, etc.

Children crying.

Hypodermic injections into any part of the body.

Arguments with other patients.

Physical exertion.

Defecation and urination (Case 11 only).

Drinking anything cold (Case 8 only).

Laughing (Case 13 only).

All of these different factors were known to Mitchell, except the stimulus of cold liquids, which was so striking in Case 8, laughing, and the irritating effects of the radio and cinema. Although Mitchell did not connect these facts, it is now obvious that the single common denominator which underlies all these diverse irritants is the burst of sympathetic impulses which are emitted under such circumstances from the hypothalamus and cause vasomotor, pilomotor, and sudomotor responses in the extremities, particularly in the areas of the hand and fingers, and in the toes and soles of the feet. These

are the areas where autonomic activity, which produces nervous sweating and vasoconstriction, is most in evidence; furthermore, these identical stimuli would produce alterations in digital blood flow, if measured by the plethysmograph.

Doupe, Cullen, and Chance[10] have gone so far as to ascribe the peculiar qualities of causalgic pain to direct cross stimulation of sensory fibers by efferent sympathetic impulses at the point where the nerve trunk is injured, rather than to the indirect action of the vasoconstrictor response which they also produce. They have cited most convincing evidence for this activation of sensory fibers by sympathetic impulses. Their theory furnishes an explanation not only for the increase in pain which so characteristically takes place in a cold environment, but also for that occurring during any form of emotional excitement, cutaneous stimulation, and, in some extreme instances, during everyday visual and auditory stimuli. Burning pain in causalgia and in certain other conditions occurs in direct relationship to the tonic vasomotor, sudomotor, and pilomotor discharge over the sympathetic efferent pathways. It is reduced in a quiet, stable environment and during sleep, when the tonic hypothalamic discharge is greatly diminished, and can be interrupted completely by tetraethylammonium bromide for as long a period as the ganglionic synapses are blocked by the drug. There is no valid evidence that the sympathetic system plays any direct role in the central conduction of the painful stimuli.

As further corroboration of this theory of sympathetic activation of sensory fibers, it has been shown by Katz and Schmitt [15] that under certain circumstances efferent nerve impulses can alter the excitability of adjacent sensory axones. Recently Granit, Leksell, and Skoglund[13] have given direct experimental proof of such cross-stimulation between motor and sensory fibers at a point of nerve injury by recording with the cathode ray oscillograph an afferent discharge from the sensory root which takes place when the motor root is stimulated. They conclude that the small, poorly myelinated pain axones of the C-group should be especially susceptible to "fiber interaction," and that this is a simple explanation for some of the symptoms of causalgia. The theory of Doupe and his co-workers assumes that the activating impulses come from the sympathetic vasomotor, pilomotor, and sudomotor discharge, which is always increased by cold or emotional excitement. A serious objection to this theory has been brought forward by Richards,[30] who points out that proximal division of the nerve has failed to relieve causalgia, although it must necessarily eliminate both the efferent and afferent arcs of the "short-circuited" area at the level of nerve injury. Possible flaws in this pertinent objection are that (1) neurectomy, which was often attempted unsuccessfully in the past, was performed at too late a date, after the painful pattern had become established in the sensory cortex (as is now known to occur after long-standing pain from a phantom limb); and (2) when a nerve trunk is involved in the causalgic state its sensory fibers may become so irritable

that a similar "short-circuiting" mechanism will be set up in the proximal neuroma after neurectomy at a higher level. Ulmer and Mayfield[39] have recently reported successful results from excision of the injured segment of nerve with immediate suture.

TREATMENT

Our experience, as well as that of other writers previously mentioned, has shown that total sympathetic denervation of a limb is an effective method for the relief of true causalgia. A single partial failure in Case 11 turned out to be due in large part to an incomplete operation. Here a limited sympathectomy of the type recommended by Atlas,[4] with removal of two ganglia at the side of the second lumbar vertebra, failed to eliminate the burning pain in the toes and anterior third of the foot, although the hyperesthesia of the proximal two-thirds was relieved. When the sympathetic denervation was completed by removing an abnormally-placed ganglion below, the residual pain in the anterior portion of the foot gradually disappeared. In another instance of slightly atypical causalgia in the hand, which we had the opportunity to observe, but which is not included in this series, there was also an early recurrence of pain after sympathectomy. In this case postoperative roentgen rays revealed that the surgeon had mistaken the fourth for the third rib and, by making his approach at such a low level, had failed to interrupt the important sympathetic efferent fibers which leave the thoracic cord in its second anterior root. It is therefore obvious that, as in every other condition which can be influenced by sympathectomy, the surgical denervation of the area concerned must be complete if it is to be effective.[43]. In view of these findings we have come to believe that, in the early typical case of major causalgia which exhibits the classical triad of symptoms described above and in which there has been temporary relief of pain following diagnostic procaine block, failure is due to incomplete sympathetic denervation. Under such circumstances residual vasomotor and sudomotor activity should be sought, not by the cruder methods of recording environmental alterations in skin temperature and gross sweating, but by the digital plethymograph[7] and changes in cutaneous resistance to galvanic current.[31]

The technical steps necessary to obtain a complete sympathetic denervation of the upper or lower extremity are described in White and Smithwick's monograph on *The Autonomic Nervous System*[43] and, with more recent modifications, in White's chapter on the surgical technic of sympathectomy in Bancroft and Pilcher's *Surgical Treatment of the Nervous System*.[40] For the relief of burning pain in the hand the preganglionic operation is best. On theoretical grounds we would have supposed that resection of the inferior cervical and upper two thoracic ganglia would have given equally effective results as far as relief of pain is concerned, but this has not been the experience of Rasmussen and Freedman.[28] In addition, the latter procedure, by causing degeneration of the postganglionic neurones, does not produce as effective vasodilatation of the hand[42] and also leaves the patient

with a disfiguring unilateral Horner's syndrone. After wounds in the lower leg removal of the second and third lumbar ganglia should ordinarily suffice, but it is best to remove a good five centimeters of the chain and carry the resection down to the lower border of the third lumbar vertebrae.* Excision of too short a length of trunk may be followed by regeneration, and our unfortunate experience in Case 11 shows that at times white rami communicantes may reach the ganglionated chain below the second lumbar vertebra.

The area of sympathetic denervation must also reach well above the level of nerve injury. Whereas the standard upper thoracic sympathectomy interrupts sympathetic impulses to the entire arm and shoulder, it must be borne in mind that after resection of the second and third lumbar ganglia the effect is limited to the foot. When the pain arises from a wound at the knee it is advisable to remove the first lumbar ganglion as well, and in cases of nerve injury in the upper thigh it may be necessary to extend the sympathectomy upwards through the diaphragm to include the lowest thoracic ganglia as well.**

In general it is wise to test the effectiveness of sympathectomy by preoperative paravertebral injection of the regional sympathetic fibers. This should stop the sense of burning and hyperpathia for a period of several hours. While procaine injection alone may occasionally produce long-standing relief in some of the minor causalgias, in painful post-traumatic arthritis and Südeck's atrophy, there are only a few cases on record[28] where it has stopped major causalgia for more than a few hours. It does, however, assure the surgeon of the successful outcome of the proposed sympathectomy and is, therefore, of particular value in cases that are in any way atypical. Possibly the recent demonstration of Rasmussen and Farr[27] that prolonged duration of chemical block can be obtained by the injection of 5 per cent benzyl alcohol propylaminobenzoate with procaine (Rectocain) may permit effective therapy by paravertebral injection alone.

The operation for causalgia in both the upper and lower extremities is simple and safe in the hands of a surgeon who is experienced in the technic of sympathetic neurosurgery. Furthermore, the postoperative period of disability is short and the patient need only spend a few days in bed. There have been no significant complications in any of these patients. There is therefore every reason to operate at an early date before the patient has become dependent on narcotics, and particularly before he has developed neurotic tendencies or irreversible atrophic changes in his bones and soft

* In performing these operations it has always been our practice to apply a dural clip to the proximal and distal stumps of the resected portion of the sympathetic trunk and to each large ramus cut. The position of these metallic markers compared with the bony landmarks in postoperative roentgenograms gives an accurate picture of the anatomic extent of the sympathetic denervation.

** While this point is not yet fully established, recent observations of Ulmer and Mayfield[39] render it highly probable.

tissues (see protocol of Case 11 above). Once the causalgic syndrome has developed with full intensity there is little, if any, hope of spontaneous remission. It has been our experience that preliminary neurolysis is totally ineffective for relief of severe causalgia, and that this procedure, if indicated, should be undertaken after the burning pain has been relieved by sympathectomy. In five of our patients (Nos. 1, 3, 7, 8, and 9) neurolysis of the injured nerve had been performed as the primary procedure (Fig. 3B), but without any influence on the causalgia. We therefore recommend primary local surgery only if there is a foreign body in contact with the nerve, a septic focus, or when the pain is so mild that the patient can bear it without too great difficulty over the long period required for complete reneurotization of the injured nerve. Ulmer and Mayfield[39] have reported that complete resection of the area of injured nerve followed by suture may be expected to abolish the pain, but as the injured nerve which produces the causalgic syndrome is rarely seriously damaged and, given time, will recover spontaneously, this radical procedure will rarely be justified.

Two final points connected with these operations are of considerable theoretical interest. These are related to the physiologic changes that follow injuries to the sympathetic and sensory fibers in the peripheral nerves:

(1) A number of our patients (Nos. 2, 3, 4 and 5) had, in addition to a partial injury of the median or ulnar nerve, complete paralysis of the other trunk. After sympathectomy under these circumstances there was complete vasodilatation only in the area of intact peripheral nerve supply, the paralyzed median or ulnar area remaining equally dry but distinctly cooler and somewhat cyanotic. The explanation for this lies, in large part at least, in the sensitization phenomenon, whereby denervated smooth muscle becomes hypersensitive to circulating adrenaline and sympathin. This, as shown by White, Okelberry, and Whitelaw[42] and by Ascroft,[3] is far more noticeable in areas where the postganglionic sympathetic neurones have degenerated. As these lie within the peripheral nerves, added interruption of the preganglionic connections by a paravertebral sympathectomy cannot result in a complete release of vasospasm. This phenomenon, which is of considerable academic interest, has been thoroughly investigated by Doupe[9] and Richards.[29] The chemical sensitivity of denervated smooth muscle to circulating sympathomimetic hormones may greatly reduce the value of sympathectomy in restoring a satisfactory circulation in Raynaud's disease, but fortunately does not vitiate its beneficial effects on pain. Here all that is necessary is the complete interruption of the efferent sympathetic discharge which arises in the hypothalamus in response to psychic and environmental factors.

(2) Although we have found that the intense burning hyperpathia of causalgia, which is increased by thermal and emotional disturbances, is effectively relieved by sympathectomy, the paresthesia and milder hyperesthesia which accompany sensory regeneration are not necessarily relieved by this operation. These abnormalities in the quality of returning sensation are of common occurrence after peripheral nerve injury; they are not gen-

erally severe, and they disappear with more complete recovery. They do not appear to be influenced in any way by hypothalamic stimulation and increase of the sympathetic discharge. The disagreeable quality of sensation during the early phase of nerve recovery has been ascribed by Trotter[37] and more recently by Bigelow et al[6] to the lack of insulating myelin sheaths around the regenerating sensory fibers, so that these naked axones function as pain fibers and react to any stimulus in an explosive fashion. Foerster,[11] on the other hand, has explained the hyperesthesia as due to a lack of sensory inhibition which maybe a normal function of the larger myelinated fibers in the posterior roots. In either case, the mild tingling and disagreeable sensations found in an area with early sensory recovery tend to disappear as the regenerating sensory fibers mature and reacquire their myelin sheaths. On careful testing and questioning of these patients we have discovered some degree of residual hyperesthesia in the areas of sensory recovery in Cases 2, 4, 6, 11, and 12. It was described as only a mild residual discomfort by four of these patients, but in Case 11 was severe enough to retard his rehabilitation.

SUMMARY AND CONCLUSIONS

1. Major causalgia, as first described by Mitchell, Morehouse and Keen,[26] follows partial injury of the mixed peripheral nerve trunks incurred in penetrating wounds with a rate of incidence somewhat under 5 per cent. The typical triad of symptoms consists of hyperpathia (a disagreeable burning pain with intense hyperesthesia in the hand or foot), trophic changes, and autonomic stigmata of excessive vasomotor and sudomotor activity.

2. The pain is aggravated to an unbearable degree by factors which increase the sympathetic discharge from the hypothalamic centers—thermal and psychic stimuli. While it may disappear with complete regeneration of the injured nerve, this process is at best so slow that the patient is liable to become addicted to morphine, suffer serious personality changes, and develop irreparable trophic disturbances in his bones, joints and soft tissues.

3. Interruption of the sympathetic outflow, preferably by preganglionic sympathectomy, is an effective method of treatment and should be performed at an early date. Preliminary chemical blocking of the sympathetic rami and ganglia by injection of procaine is a valuable diagnostic test, particularly in atypical cases. Repeated paravertebral injections have been reported to give lasting relief in some cases, but they have not been effective in our patients.

4. Sympathectomy in our hands has resulted in consistent relief of the burning causalgic pain. After operation eight patients had no further complaints of any sort. On careful cross-questioning, five had some residual paresthesia and hyperesthesia in the area of recovering cutaneous innervation. This in no way resembled the former causalgic syndrome and was identical with the usual subjective sensations that accompany nerve regeneration. It was severe enough to retard rehabilitation in only a single patient.

5. It is our opinion that relief of burning pain following sympathetic denervation is due to elimination of the efferent sympathetic discharge from

the hypothalamic centers rather than to any interruption of pain fibers. There is no good evidence for the existence of centrally conducting sympathetic axones in the peripheral nerves. Furthermore, the suffering of causalgia is relieved under circumstances in which sympathetic tone is reduced—viz., a quiet, warm environment, ingestion of alcohol, sleep, and febrile states. Recently reported work on experimental animals suggests that there may be a short-circuiting effect in the area of the injured peripheral nerve which permits direct irritation of sensory afferent fibers by efferent sympathetic impulses.

6. Thirteen cases are described which have been treated at a Naval Hospital. All were relieved of their unbearable pain and the resultant effect on their psychological status and resistance to rehabilitation was dramatic. While the period of follow-up has been usually less than a year, there is no reason to suppose that recurrent complications will occur.

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EFFECT OF VAGOTOMY AND OF DRUGS ON GASTRIC MOTILITY*†

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Renewed interest in vagotomy for the treatment of peptic ulcer dates back to the report of Dragstedt and his co-workers[1] in 1943. Since that time preliminary reports of clinical use of this procedure have been made by Grimson,[2] Moore,[3] and Walters,[4] with their associates. Each observer early noted complications following vagotomy, particularly delayed emptying of the stomach. That gastric retention occurred after vagotomy in patients has long been known. As early as 1911, Exner[5] reported secondary gastroenterostomy after vagotomy in two patients because of "ill effects of paralysis of the stomach." It is now generally accepted that varying degrees of retention develop in most patients treated by vagotomy unless a gastroenterostomy is performed. Gastric retention has led to varying frequency of secondary operations.

Dragstedt and Schafer[6] reported gastrojejunostomy necessary in three of the first 15 patients. In their first communication, Grimson et al[2] reported secondary gastroenterostomy in three of 25 patients and in a recent report,[7] in six of 56 patients. Moore and associates[3] had only one patient in 33 who had secondary gastroenterostomy. Walters and his group[4] recently presented a series of 56 using various technics and frequently draining the stomach. One patient who had vagotomy and gastroenterostomy subsequently required jejunojejunostomy for retention. Harkins and Hooker[8] had one patient out of 26 who required secondary gastroenterostomy, and Sanders[9] had one in 50. Since many of the above patients had pre-existing gastroenterostomy stomas or drainage of the stomach at the time of vagotomy, it is evident that retention requiring secondary gastroenterostomy is not an infrequent complication. Retention not requiring surgical relief may produce symptoms. Dragstedt[6] stated that although symptoms of retention do occur they are insignificant whereas Grimson[7] described persistent serious symptoms of retention in 15 of 56 patients.

Most authors have attributed this retention to changes of gastric motility. In kymographic studies after vagotomy, Thornton, Storer, and Dragstedt[10] found decreased motility and concluded that gastric hypermotility and hypertonicity of ulcer patients returned toward a normal state after bilateral vagotomy. They believed that retention is caused by decreased tone and

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emphasized suction and residual aspiration as preventive measures. Grimson et al[7] performed kymographic studies of intragastric pressures in most patients before vagotomy and in 42 patients immediately afterward. Recordings were also obtained in 34 patients between three months and one year, and in 11 between one and two and a half years. They determined that the average resting intragastric pressure of patients who had vagotomy alone for duodenal ulcer was somewhat increased after vagotomy, whereas amplitude of gastric contraction waves decreased. These changes persisted in nine patients followed more than one year. They believe that retention is caused by a disturbance of the emptying cycle of the pylorus or an achalasia-like obstruction and not by lack of resting intragastric tone. Moore, Chapman, Schulz, and Jones,[3] however, concluded that gastric motility usually decreases after vagotomy but may return to normal or nearly normal levels at the end of one year. It is evident, therefore, that there is no agreement upon the explanation of the retention phenomena.

It is not possible in this report to review completely the extensive literature, experimental or clinical, on gastric motility and the effects of vagus nerve section. Excellent summaries are provided in the papers by Ferguson[11] and by McSwiney.[12]

Since retention with delayed gastric emptying occurs frequently after vagotomy and occasionally causes serious complications, studies were started nearly two years ago in animals and in patients to find, if possible, a nonoperative means of treatment. Gastrometric methods were used for all observations.

METHOD

In rabbits, a thin rubber balloon was attached over the end of a small rubber catheter and passed into the fasting stomach. The tube was attached to a water manometer recording fluctuations of intragastric pressure on a kymograph and the balloon was inflated with an average of 25 cc. of air.

In dogs, a bromoform manometer was usually employed, the balloon being inflated with 200 cc. of air.

A similar method of recording was used in patients using a larger balloon over the end of a Levine tube connected to a bromoform manometer. Three hundred cc. of air were introduced into the balloon in increments of 50 cc. at about one minute intervals.

CHRONIC EXPERIMENTS ON VAGOTIMIZED ANIMALS

Fifty rabbits were subjected to vagotomy through a left thoracotomy incision using positive pressure ether anesthesia. The esophagus and vagus nerves were freed, a 2 cm. section of each nerve was removed, and smaller fibers if found were excised. Satisfactory postoperative recordings of gastric motility were obtained from eight hours to one year after operation in 26 rabbits.

Results of these studies are shown in Table I. It was hoped that vagotomy would produce a hypomotile stomach comparable to that seen in patients after vagotomy, in order that action of drugs which might restore contractions

could be studied. However, hypermotility usually developed and animals could not be used for this purpose. The arithmetic mean of the height of contractions preoperatively was 3.48 cm. of water, and postoperatively 4.8 cm. The arithmetic mean of the frequency of contractions preoperatively was 11.6 contractions per ten minute intervals and post-operatively was 19.9. A typical contrast between effect of vagotomy in patients and in rabbits is illustrated in Figure 1. Several observations in these animals, however, appear worth recording.

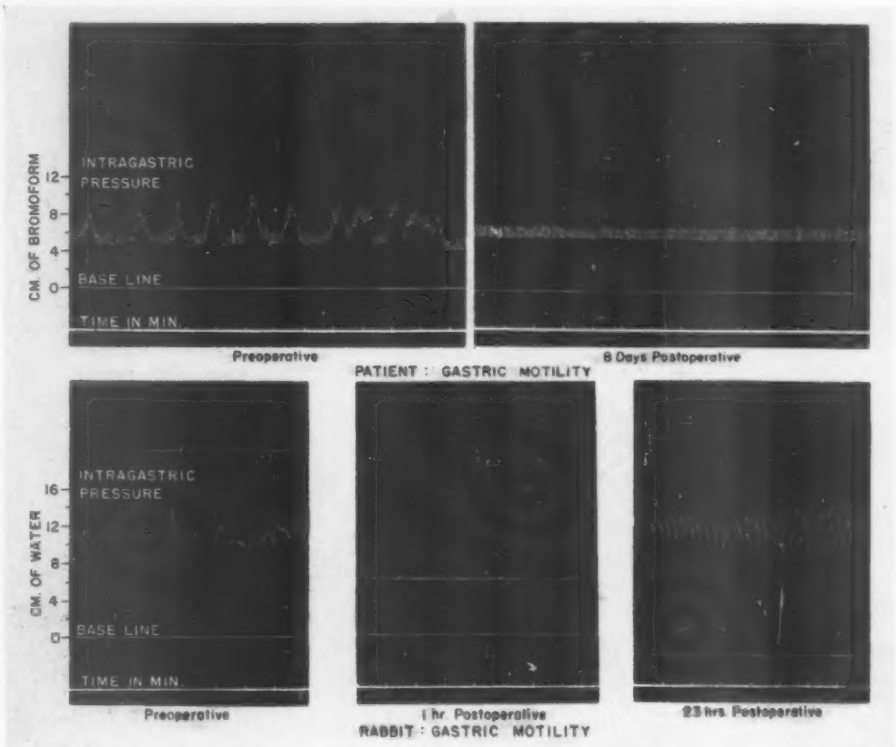

FIG. 1.—Tracings of fluctuations of intragastric pressure of a patient and of a rabbit are contrasted. Marked fluctuations occurred in the patient before vagotomy (upper left) and ceased afterward (upper right). Fluctuations of the rabbit (lower left) ceased during the first few hours after vagotomy (center) but by 23 hours (lower right) spontaneously became frequent and exaggerated.

Completeness of transthoracic vagotomy was tested two weeks or more after operation by acute experiments in 6 rabbits. Balloon study showed typical high rapid hypermotile waves at the start of each acute experiment. The vagus nerves were then again sectioned, this time in the neck, using local anesthesia. Hypermotility was not altered. Also, electrical stimulation of distal ends of the divided vagi produced no change. Atropine, 0.1 to 0.3 mg., given subcutaneously during recording of hypermotility in three other animals effected cessation of hypermotility. In one after 20 minutes and in another after 30 minutes motility ceased. In the third there was a marked decrease

TABLE I.—*Gastric Motility in 26 Rabbits After Transthoracic Vagotomy*

	Time After Operation			
	0 - 48 Hours	2 - 7 Days	8 - 30 Days	1 - 12 Months
No. Tests	9	19	21	15
Absent Motility	4	3	1	1
Normal Motility	4	12	2	5
Hypermotility	1	4	18	9

of contractions in 30 minutes. Two units of pituitrin were given intravenously to three other rabbits with hypermotility. This caused immediate loss of resting tone and cessation of contractions lasting six to ten minutes.

Three to ten units of insulin were given intravenously during recording of hypermotility in four additional rabbits surviving transthoracic vagotomy. Motility promptly stopped in each. Hypermotolity returned after about 25 minutes and during the period of hypoglycemia. In one of these animals hypermotolity developing after 25 minutes was slightly greater than that present before injection of insulin. Intravenous administration of 50% glucose in water a half hour or more after insulin and during the period of hypoglycemia stopped all motility. Control animals with intact vagi showed similar reactions to insulin hypoglycemia except that normal motility present before insulin increased during the period of hypoglycemia.

Autopsies were performed on most of the rabbits surviving transthoracic vagotomy. Grossly there was no evidence of overlooked nerves. Stomachs were uniformly markedly enlarged and contained huge quantities of sour greenish semi-solid residue. Gastric ulcers were present in one-fifth of the animals.

Transthoracic vagotomy was also performed on two dogs and their gastric motility was observed for two months. Complete emptying time of the stomachs was decreased, as judged by passage of barium seen fluoroscopically. Kymographic studies, which had revealed resting intragastric pressures of 38 to 40 mm. of bromoform and moderately irregular contraction patterns with rate varying from one to four per minute and excursions varying from 8 to 44 mm. of bromoform during three tests on each dog before vagotomy were definitely altered afterward. Average resting intragastric pressures after vagotomy were 57 and 69 mm. of bromoform. With two exceptions the pattern was markedly irregular. Frequency varied from one to six per minute and excursions ranged from 4 to 100 mm. of bromoform during 13 one- to two-hour balloon studies run at intervals of several days to two months. The two exceptions occurred at 16 and 39 days and differed in that contractions were regular, excursions varying from 2 to 4 mm. of bromoform and frequency varying from three to four per minute. At autopsy these two dogs weighing 10 and 12 kg. respectively had stomachs markedly distended, filling nearly half the abdomen. The volume of one stomach was 550 cc. and of the other 700 cc. Ulcer was not found in either.

Since these attempts to produce satisfactory chronic preparations with hypomotile stomachs failed in both rabbits and dogs, observations were carried

out to study gastric motility during the first 12 hours after cervical vagotomy and to determine effects of drugs during this period.

ACUTE EXPERIMENTS ON VAGOTOMIZED RABBITS

Observations were made in 48 rabbits before and during the first 12 to 48 hours after cervical vagotomy. Cessation of gastric contractions always occurred. Animals seldom survived more than 48 hours, usually dying with respiratory infections. Each of six that survived developed hypermotility

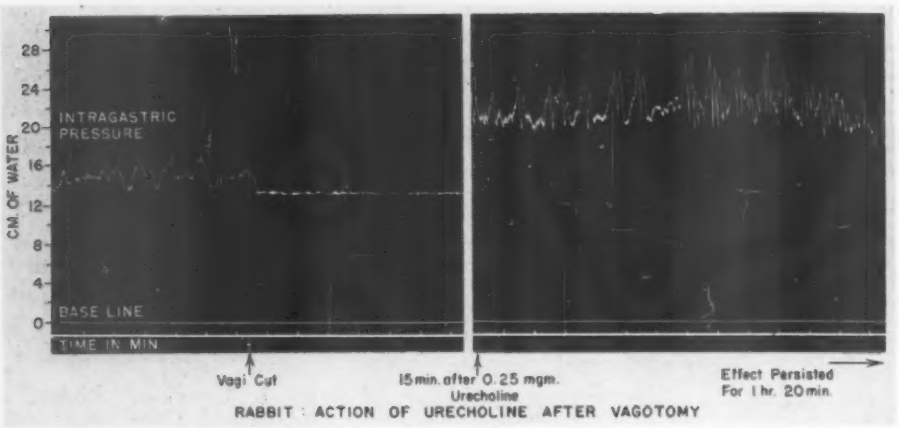

FIG. 2.—Gastrometric tracings illustrating immediate effect of vagotomy (left) and increase of tone with restoration of forceful contractions (right) 15 minutes after intramuscular injection of urecholine.

like that described above under chronic experiments on vagotomized animals.

During the 12 to 48-hour period of absent motility after cervical vagotomy, insulin hypoglycemia in seven animals did not restore motility during two to nine hour periods of continuous observation. Also, gastric hypermotility produced by insulin hypoglycemia in four normal animals was immediately and completely abolished by cervical vagotomy performed one half to one hour after injection of insulin.

Drugs other than insulin were also given during the 12-to-48 hour period of absent motility. These drugs and their effects are summarized in Table II. Of the drugs used, pilocarpine, Doryl and Urecholine produced most effective restoration of contractions. A typical effect of Urecholine is illustrated in Figure 2.

STUDIES ON PATIENTS BEFORE AND AFTER VAGOTOMY

Before vagotomy four drugs were given during gastrometric study periods in 19 patients. Each patient had a peptic ulcer to be treated by vagotomy. Eight tests with Prostigmine (0.5 to 1.5 mg. subcutaneously), four with Mecholyl (0.2 Gm. orally), and four with Doryl (0.15 to 0.25 mg. subcutaneously or 2.0 mg. under the tongue) failed to alter frequency, or pattern of contractions. Urecholine (10 mg. under the tongue) had no effect in two

TABLE 2.—*Effect of Drugs on Gastric Motility in Rabbits After Cervical Vagotomy*

Drug	No. of Animals	No. of Tests	Effective Dose	Increase of Tone	Restoration of Contractions
Pilocarpine	4	4	3.0 mg.	2 - 4 cm.*	4 - 6 cm.
Histamine	4	6	0.5 mg.	0 - 2 cm.	0 - 2 cm.
Prostigmine	5	6	0.2 mg.	0 - 2 cm.	2 - 4 cm.
Mecholyl	9	18	2.0 mg.	0 - 2 cm.	2 - 4 cm.
Doryl	9	17	0.02 mg.	2 - 4 cm.	4 - 6 cm.
Urecholine	7	12	0.25 mg.	0 - 2 cm.	4 - 6 cm.

* cm. of water.

patients and was followed by slight increase of contractions in one. A similar slight increase was produced in another by 2.5 mg. subcutaneously.

Experimental observations of the effect of drugs were obtained in 91 instances, using patients at intervals of seven days to two and a half years after transthoracic vagotomy. During 15- to 60-minute periods of observation before administration of drugs, motility was absent in most patients and abnormally low in all. The postoperative tracing in the upper half of Figure 1 is typical. Drugs to be tested were then administered and observation recorded for several hours. Subcutaneous injection of 0.5 to 2.0 mg. of Prostigmine was employed in 21 tests on 16 patients. It was without demonstrable effect on gastric motility. Other drugs produced varying effects abstracted in Table III.

Mecholyl (acetyl-beta-methyl-choline chloride or bromide) was given to nine patients, Table IIIA, and only occasionally produced slight contractions without increase of tone. Doryl (carbamylcholine chloride) was given to ten patients and found more effective (Table IIIB). Excellent contractions were occasionally observed following 2.0 mg. of Doryl swallowed or placed under the tongue. In all, eight of the ten patients had contractions and only two had no effect. Significant side effects were not observed.

While Doryl was being studied, Machella, Hodges and Lorber[13] suggested that Urecholine (urethane of beta-methyl-choline chloride) might prove effective, as they had obtained good results in two patients. Effects produced by Urecholine are summarized in Table IIIC and the response of two patients shown in Figure 3. Administered subcutaneously to eight patients, it produced good contractions in each with increase of tone in four. Given orally or dissolved under the tongue, small doses (5 to 30 mg.) usually had no effect. Thirty milligrams under the tongue increased motility in three of seven patients. Restoration of contractions and increase of resting tone were most consistently produced by oral or sublingual administration of 40 to 50 mg. Side effects were insignificant; mild symptoms of flushing, sweating, and salivation occurred occasionally with these larger doses but were not troublesome.

DISCUSSION

It seems apparent that the changes of gastric motility after vagotomy in rabbits and dogs differ from those observed in man. Hypermotility was usually produced in these animals and hypomotility in man. Gastric retention, how-

TABLE 3.—*Effect of Mecholyl, Doryl and Urecholine on Gastric Motility in Ulcer Patients Treated by Vagotomy*

Dose	No. of Tests	Tone		Contractions		Height of Contraction	Time of Onset (Min.)
		No Change	Increased	No Change	Restoration		
A. Mecholyl							
1. Subq.							
10 mg.	2	2	0	0	2	0 - 2 cm.*	1 -2
2. Orally							
0.2 Gm.	7	7	0	5	2	0 - 2 cm.	10 - 15
B. Doryl							
1. Subq.							
0.15 mg.	1	1	0	1	0	—	—
0.25 mg.	1	1	0	0	1	0 - 2 cm.	20
2. Under Tongue							
2.0 mg.	7	5	2	1	6	2 - 6 cm.	30 - 75
3. Orally							
2.0 mg.	1	0	1	0	1	6 cm.	90
C. Urecholine							
1. Subq.							
1.0 mg.	2	2	0	0	2	0 - 2 cm.	2 - 5
2.0 mg.	1	1	0	0	1	2 - 4 cm.	10
2.5 mg.	4	1	3	0	4	4 - 6 cm.	2 - 10
5.0 mg.	1	0	1	0	1	0 - 2 cm.	4
2. Under Tongue							
5.0 mg.	1	1	0	1	0	—	—
10.0 mg.	3	3	0	2	1	0 - 2 cm.	50
20.0 mg.	1	0	1	0	1	2 - 4 cm.	145
30.0 mg.	7	7	0	4	3	2 - 4 cm.	60 - 120
40.0 mg.	1	1	0	0	1	0 - 2 cm.	150
50.0 mg.	2	0	2	0	2	2 - 4 cm.	150 - 210
3. Orally							
10.0 mg.	1	1	0	1	0	—	—
50.0 mg.	1	0	0	0	1	2 - 4 cm.	120

*cm. of bromoform.

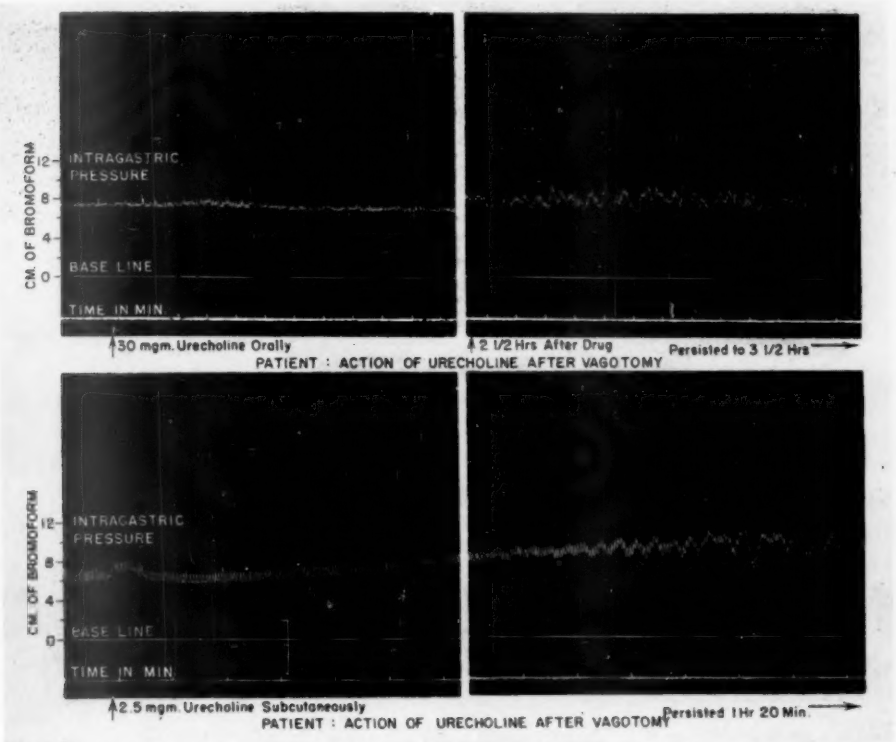

FIG. 3.—Restoration of fluctuations of intragastric pressure in 2 patients treated by vagotomy and then 3 weeks and 3 months later given urecholine orally (above) and subcutaneously (below).

ever, occurs in rabbits and dogs without scar tissue from ulcer and in patients with duodenal or gastric ulcer. Discussion of differences in motility, similarity in retention, and similarity in drug action will be presented separately.

Although development of hypermotolity in animals after 12-48 hours made investigation of drug action difficult, it nevertheless represents a phenomenon, the explanation of which may have clinical significance. Ophuls[14] and Auer[15] first reported return of motility in rabbits after vagotomy and this has subsequently been confirmed by several observers. In our experiments return of motility in rabbits has been evidenced by contractions of excessively high amplitude occurring with abnormal rapidity.

Vanzant[16] recently reported changes of motility and secretions in dogs followed ten to 57 months after vagotomy. In seven of eight dogs, emptying time returned to normal and in one there was increased emptying. It is not clear whether she means initial emptying time or time of complete emptying. It is generally difficult in the literature to separate accounts of emptying time based upon initial emptying from those based upon complete emptying.

Regardless of the type of observation it is generally stated that some degree of recovery of motor activity occurs. Vanzant suggested that return of motility might be due to: (1) regeneration of the severed nerves, (2) assumption of

stimulatory function by splanchnic parasympathetic fibers or (3) spontaneous restoration by an intrinsic mechanism in the stomach. The first assumption was thought unlikely since sections of the stomachs showed degenerated nerve fibers. The second was thought not applicable since secretions and motility returned when both vagi and splanchnics were served. She therefore felt that the third explanation, restoration by intrinsic mechanism, was most likely.

It is evident from our observation and those of others that nerve regeneration could not explain return or recovery of motility within one or two days. Also, it was found in our acute experiments on previously vagotomized animals that cutting or stimulating the vagus nerves in the neck had no effect on gastric motility, thus establishing completeness of the transthoracic vagotomy and ruling out recovery by overlooked nerve fibers or regeneration. In these animals vagotomized for two weeks or more insulin produced cessation of motility for half an hour like that observed in normal rabbits. Subsequent restoration of motility, however, was equivalent to that before insulin and not to the hyperactive level seen in normal animals. It would appear therefore that the immediate action of insulin is inhibition of motility and that this action occurs whether the vagi are intact or absent. Also, it would appear that hypermotility occurring a half hour or more after insulin in normal rabbits does not recur after transthoracic or cervical vagotomy. Extravagal parasympathetic pathways if present apparently cannot mediate this hypermotile response.

The explanation of spontaneous restoration of motility in animals after both vagotomy and splanchnicectomy, by intrinsic mechanisms of the stomach rather than regeneration, or extravagal pathways may not apply to humans. It is still interesting to speculate that the difference observed in patients both in motility and response to insulin hypoglycemia might be related to presence or effectiveness of extravagal pathways.

A difference exists between animals and man that might be related to the different results of vagotomy on motility. Van Yzeren[18] in 1901 reported development of gastric ulcers in rabbits after vagotomy, and this was early confirmed by others.[14, 15] In man, after vagus section, gastric hypomotility occurs and persists for at least 2½ years as judged by 300 cc. balloon manometric methods. It is generally accepted that vagotomy causes healing of ulcers in patients. Therefore, after transthoracic vagotomy in rabbits, gastric hypermotility and occasionally ulcer formation occur, whereas after the same procedure in man, gastric hypomotility and healing of ulcer are produced.

Prolonged or excessive retention of gastric content and distention of the stomach occurred in rabbits. Efforts to empty completely the stomach by starvation, liquid diet, lavage, or gastrostomy usually failed. Retained food or secretion may have played a role in the hypermotility described.

Gastric retention also occurs in patients. This manifests itself clinically even though suction is continued four or five days and occurs as soon as light feedings are given. Delayed emptying is associated with decreased gastric motility and may not be the same in all patients. One explanation of retention

in patients after vagotomy is atony. Our measurements of resting intragastric pressure, however, show little change or increase of tone. A second explanation is that scarring about the ulcer may cause obstruction. Retention, however, is found in patients with or without ulcer. A third theoretical explanation of retention may be pylorospasm. A fourth more plausible explanation is derangement of the ejection cycle of the stomach. Normally, during digestion a peristaltic wave passes down through the antrum and separates a bolus of food from the main mass. The pylorus then relaxes and the bolus passes through. After vagotomy this "biting off" of a bolus does not occur as observed fluoroscopically, and the propulsive action of the diminished peristaltic waves mechanically fails to carry food through the pylorus. Since retention occurs in animals without ulcer and with hypermotility of an abnormal sort it would appear that pylorospasm or failure of the ejection cycle is an important factor causing obstruction, retention and dilatation.

If the explanation by faulty ejection cycle is correct, then stimulation of peristalsis by drugs during the postprandial period might produce satisfactory emptying. The studies reported show that subcutaneous injection of Doryl or Urecholine will produce contractions of amplitude and frequently equal to or greater than those seen preoperatively, as judged by intragastic balloon studies. Doryl or Urecholine dissolved under the tongue or given orally will cause similar contractions, although usually the onset is delayed. That Urecholine will cause increased peristalsis and prompt emptying of the stomach of vagotomy patients has been demonstrated fluoroscopically by Machella, Hodges and Lorber;[13] by Grimson and co-workers,[7] and by others.

Decreased or abnormal motility, therefore, seems to be the cause of retention, and faulty motility and retention can both be corrected by injection of drugs. Maintained treatment of vagotomized patients with retention by Urecholine however, although partially effective, has not eliminated necessity for occasional secondary drainage operations.

CONCLUSIONS

1. In rabbits, cervical or transthoracic vagotomy is followed by cessation of motility for 12-48 hours and subsequently by development of abnormal hypermotility and retention.

2. Insulin hypoglycemia produces arrest of motility followed by hypermotility. The hypermotility is promptly abolished by cervical vagotomy.

3. In rabbits during the 12-48 period of absent motility after cervical vagotomy, insulin hypoglycemia fails to restore motility.

4. During the subsequent period of hypermotility, several days after transthoracic vagotomy in rabbits, insulin abolishes motility for about half an hour following which there is restoration of motility like that before insulin.

5. During the first 12-48 hours after cervical vagotomy in rabbits, the choline derivatives and pilocarpine effectively restore contractions.

6. In ulcer patients following vagotomy decrease of amplitude of gastric contractions occur, as judged by 300 cc. balloon techniques but resting intragastric pressure usually slightly increases.

7. Doryl and Urecholine may restore amplitude and frequency of gastric contractions of vagotomized patients toward normal.

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PURE SERUM ALBUMIN COMPARED WITH CITRATED PLASMA IN THE THERAPY OF CHRONIC HYPOALBUMINEMIA*†‡

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WHEN PURE HUMAN ALBUMIN in 25 per cent solution became available for civilian use, we injected some of this material intravenously in patients with nutritional hypoalbuminemia. In our very first trials we found that it produced a significant elevation of the albumin concentration of the blood in contrast to the relative ineffectiveness of plasma transfusions. Several explanations were advanced, including the possibility that the pure albumin did not participate in the protein metabolic pool and therefore remained in the circulation longer than the intact albumin molecule present in the plasma. However, it seemed important to study this difference, particularly in relation to changes in plasma volume. We therefore set up a series of clinical experiments in which comparable injections were made in the same patient and variations carefully noted in the hematocrit, the fractional protein plasma concentration, blood and plasma volume and venous pressure. As a result of these studies we found that the pure albumin leads to a more lasting increase of albumin concentration because its effect on plasma volume is transient as compared with plasma. Other differences were also observed and will be described.

PREVIOUS OBSERVATIONS

Concentrated solutions of pure human albumin were made possible because of the extensive research by E. J. Cohn and his collaborators[9] on the fractionation of human plasma which was collected and processed in large amounts by the American Red Cross during the past war. Considerable clinical investigation[10, 12, 16, 17, 21, 22, 33, 34, 36, 37, 39, 40, 43] has been carried out with this solution in patients, most of them suffering from shock or various types of hypoalbuminemia. These studies have shown that 25 Gm. of pure albumin is apparently equivalent in colloidal osmotic effect to 500 cc. of plasma and that each gram of albumin holds an average of approximately 18 cc. of water in the circulation. After injection most of the albumin was found to leave the circulation, but this was more pronounced in the chronic cases than in patients with

* The serum albumin used in this study was processed by the American National Red Cross from blood which it collected from voluntary donors.

This is one of a series of investigations on serum albumin being carried out with material supplied by the American National Red Cross. As soon as sufficient data become available to justify final conclusions concerning its therapeutic value, a full report to the medical profession on the use of serum albumin in medical practice will be published.

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shock. Attempts to correct hypoalbuminemia in nephrosis and cirrhosis were successful only when large amounts of albumin were injected.

Clinical experience with plasma has been fairly extensive, particularly as a blood substitute. It has also been used in patients with chronic hypoproteinemia, largely due to nephrosis. Pooled plasma as such or diluted with saline or glucose, as well as two to four times concentrated plasma (made up from the lyophilized or dry material) has been employed. Serum rather than plasma has also been used and with better effect, according to some observers.[1] In general the results were disappointing in patients suffering chronic depletion

TABLE I.—*Summary of Patients Studied*

Patient	Age	Sex	Diagnosis	Number of Injections Albumin	Plasma	Reactions
1. A. D.	64	M	Ulcerative Colitis	1	—	See Text
				4	—	None
				—	1	Chills and fever
2. H. C.	69	M	Cirrhosis of Liver	2	—	None
				—	2	None
3. L. B.	84	F	Carcinoma of Gallbladder	1	1	None
4. B. P.	60	M	Jejunal Ulcer	1	1	None
5. A. L.	43	M	Bronchiogenic Carcinoma	2	1	None
6. M. W.	36	M	Fracture of Spine	1	1*	None
7. W. A.	70	M	Carcinoma of Pancreas	1	1	None
8. J. C.	66	F	Carcinoma of Stomach	1	1*	None
9. E. R.	75	M	Carcinoma of Pancreas	1	—	None
10. G. H.	45	F	Non-tropical Sprue	—	1	Chills and fever
				3	—	None
11. B. P.	48	M	Cirrhosis of Liver	2	—	None
12. B. S.	71	M	Carcinoma of Pancreas	2	—	None
13. H. M.	71	M	Gastric Ulcer	1	—	None
14. P. B.	55	F	Stricture of Common Duct	1	—	None
15. E. N.	30	F	Carcinoma of Sigmoid	1	—	None
16. M. F.	54	F	Carcinoma of Pancreas	1	—	None
17. L. W.	66	M	Carcinoma of Stomach	1	—	None
18. C. L.	42	M	Arachnoiditis	1	—	None
19. M. M.	79	F	Intestinal Fistula	1	—	None
20. G. S.	71	M	Cirrhosis of Liver	—	1	Chills and fever
21. J. A.	66	M	Carcinoma of Hypopharynx	—	1	None
22. W. B.	56	M	Gastric Ulcer	—	1*	None
Total				29	13	

* Pooled plasma from blood bank.

of plasma proteins, though success was claimed by some. Reactions following plasma and serum transfusions have been described as similar to those previously noted with blood. More recently pooled plasma has been found to transmit homologous jaundice even when lyophilized. This condition has not thus far been observed following the use of pure albumin prepared from pooled plasma; apparently the virus responsible for the disease is destroyed in the preparation of pure albumin.

METHODS AND PROCEDURES

Twenty-two patients were selected for study, as listed in Table I. They all were malnourished and showed a fall in the level of plasma albumin. The diagnoses included a variety of conditions, but none had nephrosis. Moreover, in only three, possibly four cases, was hepatic disease present and

responsible perhaps for some degree of impairment in albumin synthesis. Aside from these cases which also presented a history of food deprivation, it was assumed that the hypoalbuminemia was largely if not wholly of nutritional origin. With one exception, no patient showed any evidence of cardiac insufficiency.

All patients were observed for several days before study. Ample fluid intake was assured and vitamins given by either the oral or parenteral channel. Salt deficiencies were also corrected. In most cases whole blood had been injected to correct anemia.

The plasma used was prepared double strength by dissolving two units of lyophilized Red Cross plasma with one unit of distilled water. This made a volume of 600 cc. which was injected within 30 to 40 minutes. In three patients (Table 1) comparable amounts of pooled (unconcentrated) plasma from the Barnes Hospital blood bank were used. The findings were no different from those with the lyophilized plasma.

The 25 per cent albumin solution was injected without dilution. It had special physical and chemical properties, described in detail by Cohn and his co-workers.[5, 6, 9, 29, 30, 31, 42] First of all it was salt-poor, containing but 0.2 Gm. of sodium as sodium acetyltryptophane per 100 cc. of the 25 per cent solution. It also contained 0.1 molal isoleucine. These not only rendered the solution isotonic, heat stable (so that sterilization for 10 hours at 60° Centigrade could be carried out without need for preservatives), but also completed its essential amino acid composition (so that rat growth could be maintained on a diet containing no other source of nitrogen). Its low sodium content is to be contrasted with that in 500 cc. of plasma, which contains over ten times as much (2.1 Gm.)[31]

In nine patients both pure albumin solution and plasma were injected, the amount of albumin being the same in each case. In ten cases albumin only was given. The remaining three cases received plasma alone. Several days were allowed to elapse between repeated injections.

Collection of Blood. Previous to each injection a sample of heparinized blood was removed from the antecubital vein without stasis, the patient having been in the supine position. The importance of this position has been indicated by several observers.[27, 35] Successive samples were withdrawn five minutes after the end of the injection and thereafter at intervals of 1, 3, 6 and 24 hours. The red cells were separated from the plasma by transferring a portion of the blood to an 8 mm. diameter hematocrit tube and centrifuging at a rate of 3000 revolutions per minute for 40 minutes. The hematocrit value was recorded and the plasma carefully removed. Total and fractional protein determinations were made by the colorimetric method of Weichselbaum[41] which provides a direct measure of the amount of protein in the samples by the intensity of the color produced by a copper tartrate reagent. This biuret method was compared with the traditional nitrogen determinations (Kjehldahl) and excellent checks were obtained. As a further check

on the method, a sample of human albumin solution of known concentration was analyzed and good agreement was found. Fractionation of the plasma proteins was accomplished by a modification of the Howe sodium sulfate method as described by Campbell and Hanna.[8]

Calculation of Plasma Volume. The initial plasma volume was calculated in each case and was based upon the changes in plasma albumin concentration and hematocrit following the injection of a known amount of human albumin according to the following formula.

$$PV_1 = \frac{(\text{Gm. alb. injected}) \times 100}{A_2 \quad \frac{(H_1)}{(100 - H_1)} \quad \frac{(100 - H_2)}{(H_2)} - A_1} \qquad (1)$$

PV_1 = plasma volume before injection, in cc.
A_1 = concentration of plasma albumin before injection, in Gm. per cent
A_2 = concentration of plasma albumin after injection, in Gm. per cent
H_1 = hematocrit before injection, in per cent
H_2 = hematocrit after injection, in per cent

Subsequent changes in plasma volume were estimated from changes in the hematocrit alone according to the following formula.

$$PV_2 = PV_1 \frac{(H_1)}{(100 - H_1)} \frac{(100 - H_2)}{(H_2)} \qquad (2)$$

PV_2 = plasma volume after injection in cc.
PV_1 = plasma volume before injection, in cc.
H_1 = hematocrit before injection, in per cent
H_2 = hematocrit after injection, in per cent

Formulas 1 and 2 are based upon the following assumptions: (1) all of the injected albumin remains in the circulation during the period of injection; (2) the mass of the total circulating red blood cells remains constant.

To check these assumptions, plasma volume before and after the injection of albumin or plasma was measured simultaneously in several cases by the method in which a sample of the patient's red blood cells labeled with radioactive phosphorus was used. These data (to be published in a separate communication) indicated that the initial plasma volume calculated from Formula 1 is usually too high by about 500 cc. This discrepancy is undoubtedly due to the escape of some of the injected albumin from the circulation during the period of injection. The longer the period of injection the greater will be the discrepancy. However, the subsequent changes in plasma volume as calculated from Formula 2 were in close agreement with those obtained by the radioactive phosphorus technic. Moreover, the assumption that the total amount of circulating red blood cells remains constant was also borne out by calculations based upon radioactive phosphorus technic.

Determination of the pulse rate, respiratory rate, arterial blood pressure and venous pressure (method of Moritz and Von Tabora) were made before and after the injection of one-fourth, two-fourths, three-fourths and all of the respective solutions. The venous pressure was determined through the same needle (18-gauge) as the solution was being injected by means of a three-way stopcock. The general condition of the patient, febrile reaction and local reaction were carefully checked before and after injection.

The possibility of variations in the water content of the red blood cells was studied by calculation of the mean corpuscular volume, mean corpuscular hemoglobin and mean corpuscular hemoglobin concentration from the hemoglobin

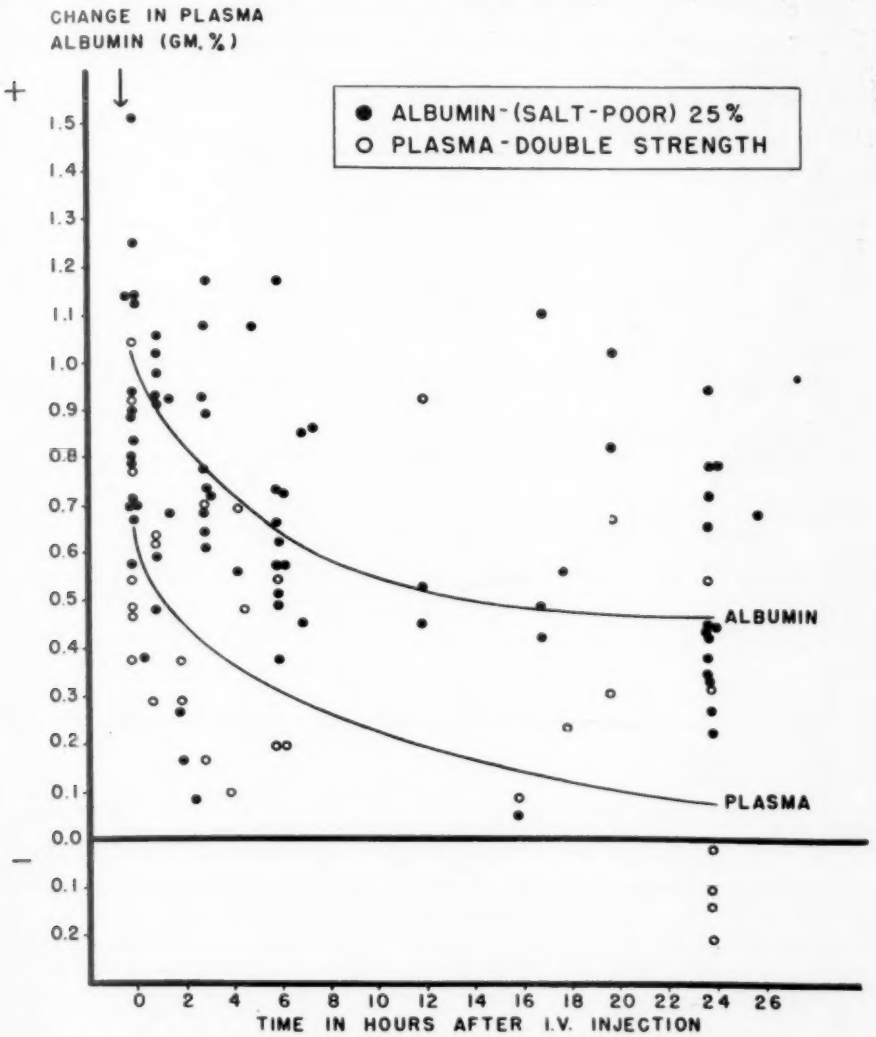

FIG. 1.—CHANGES IN PLASMA ALBUMIN CONCENTRATION.—Each point represents a determination showing the change in concentration of plasma albumin following the injection of a 25% salt-poor human albumin solution and of double strength plasma. The two curves were plotted from mean values in each group. Statistical analyses of these curves show a significant difference in the values at 24 hours. Note the rate of return of the albumin concentration to the preinjection level in the case of plasma in contrast to its more sustained level (average +0.5 Gm. %) in the case of pure albumin injections.

concentration (as determined by the use of the photoelectric clorimeter calibrated for oxyhemoglobin) and the hematocrit.

The twenty-four-hour urine specimens following injection were tested for

albumin by means of heat and acetic acid test and trichloracetic acid precipitation.

FINDINGS

The changes in the concentration of albumin following both the injection of 25 per cent pure human albumin and of plasma were plotted as a scatter

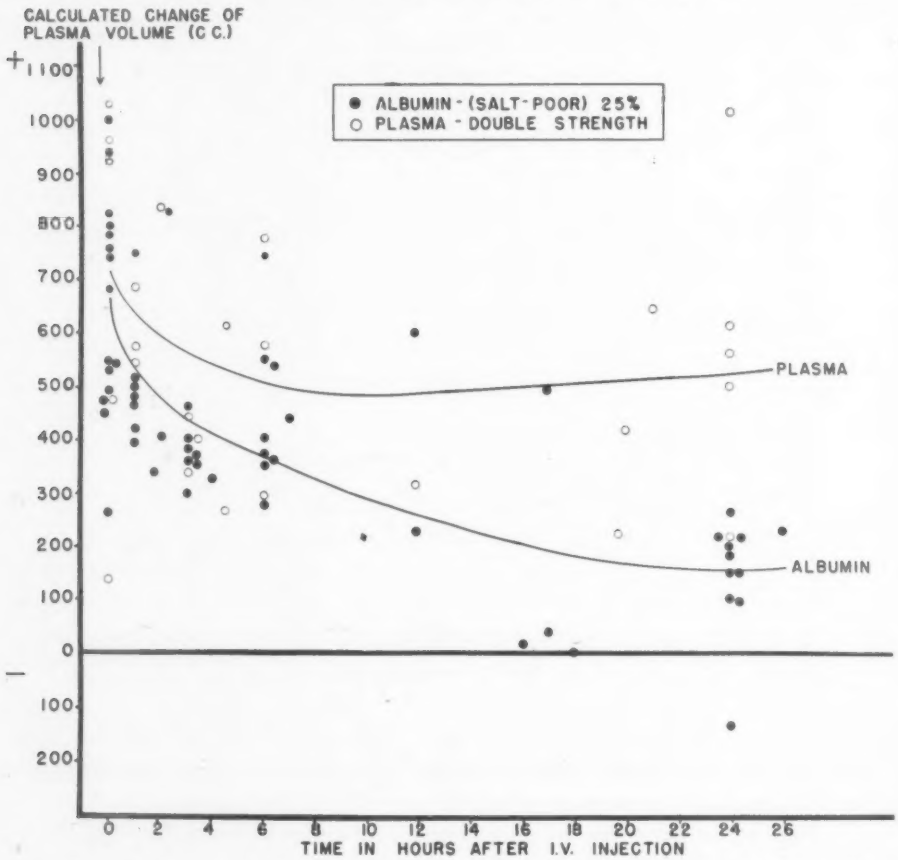

FIG. 2. CHANGES IN PLASMA VOLUME.—Each point represents a determination showing changes in plasma volume as calculated from formulas 1 and 2 (see text) following the injection of a 25% salt-poor human albumin injection and of double strength plasma. The two curves were plotted from mean values in each group. Statistical analyses of the curves show a significant difference in the values at 24 hours. Note the rapid return to the preinjection level in the case of pure albumin injection, in contrast to its more sustained level (average + 500 cc.) in the case of plasma transfusions.

diagram in Figure 1, and a curve, representing the mean change, calculated from these data. It will be obvious on consulting this figure that the initial rise in the concentration of plasma albumin which followed the injection in each case fell fairly rapidly, but that it returned to the initial level only in the case of the plasma injections.

In Figure 2 is a similar scatter diagram recording the changes in the plasma volume in the two groups of injections. Here it will be noted that

the initial increase in the plasma volume produced by each injection also fell during the subsequent 24 hours, but that the fall had produced a return to the initial level in case of the pure albumin, whereas with plasma there was still a significant increase at that time.

These differences are strikingly shown in Figure 3, which records the findings in a single typical case in which successive injections of albumin and plasma were given. Here it can be seen that the albumin concentration 24 hours after the injection of 25 per cent albumin solution is significantly higher

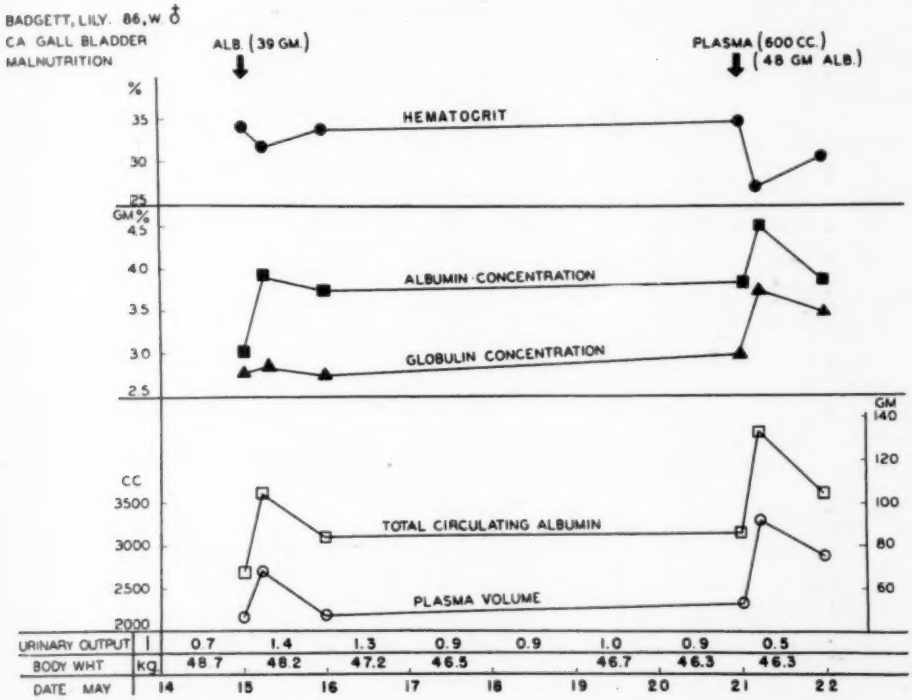

FIG. 3.—Observations made on a patient receiving both salt-poor albumin and double strength plasma at an interval of 6 days. Note the similarity in total circulating albumin. Note, however, that plasma produced a greater increase in plasma volume at 24 hours with no change in the concentration of albumin in contrast to the effect of the pure albumin solution which resulted in no change in plasma volume but a sustained increase in the concentration of albumin. Note also that the albumin produced a greater diuresis and a fall in body weight compared to the plasma.

than that following the injection of double strength plasma containing larger amounts of albumin. That this is the result of a more sustained increase in the plasma volume following plasma injection than that following albumin injection is likewise apparent, the changes in total circulating albumin being approximately equal.

That there was no change in the size of the red cell during our study is shown by the similarity of the curves in Figure 4. These curves record, in a typical case, the rate of disappearance of injected albumin (in per cent) as calculated from changes in both hematocrit and hemoglobin concentration

following injection. Moreover, no significant change was found in the mean corpuscular volume, mean corpuscular hemoglobin, or mean corpuscular hemoglobin concentration of the red blood cells of other patients receiving either concentrated human albumin or double strength plasma.

Of incidental interest is the behavior of albumin following repeated injections. In Figure 5 is recorded the disappearance curve of albumin following successive injections at intervals of several days in the case of both 25 per cent albumin solution and double strength plasma. The curves are based on the

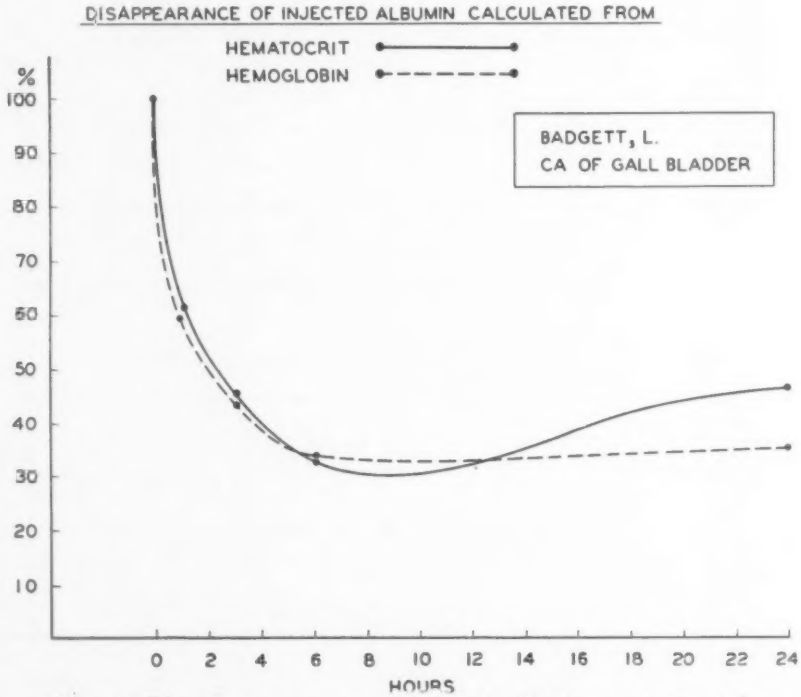

FIG. 4.—Disappearance curves of injected albumin as calculated from formulas 1 and 2 (see text) based upon both the hematocrit and hemoglobin measurements. Note that both curves are superimposable, thus showing that the red cell size was unchanged.

changes in the total circulating albumin calculated from its concentration and plasma volume. Apparently there is a greater retention of albumin in the blood as successive injections are given, either as double strength plasma or pure albumin.

Reactions. There was no significant change in pulse rate to respiratory rate in the absence of any reaction to the injected solution. However, there was a slight tendency toward an increase in pulse pressure in most cases. Increases in venous pressure were considered to be significant of an untoward effect. During five albumin injections the venous pressure was measured and only once was there an increase (from 100 to 230 mm. of isotonic saline). It was during an acute phase of the patient's illness when there was evidence of

cardiac failure. Subsequently albumin injections produced no increase in venous pressure in this patient. By contrast, in all six plasma transfusions in which venous pressure was measured, increases were noted. In three caes the pressure rose to 135, 140 and 152 mm. of isotonic saline. In the other cases severe pyrogenic reactions occurred and in them the pressure rose to 200, 300 and 310. In the majority of the cases in which the venous pressure rose during or after injection of either solution there was a slight further increase in venous

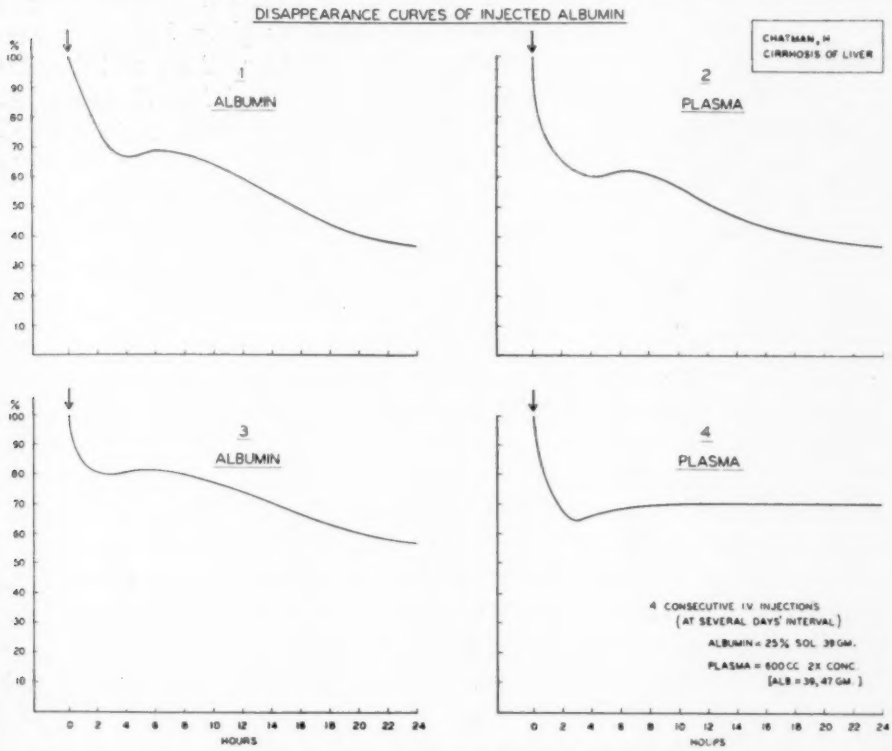

FIG. 5.—Disappearance curves of injected albumin following alternate infusions of a pure salt-poor albumin solution and of double strength plasma at several days interval, as calculated from formulas 1 and 2 (see text). Note that the disappearance rate diminishes with each successive injection.

pressure with feeling of pressure in the right upper quadrant of the abdomen.

Pyrogenic reactions were seen in three of the 13 plasma injections, none in the 29 injections of pure albumin. (Table I.) The reaction following plasma in one case was severe, with sudden dyspnea, orthopnea, pain in the retrosternal region and epigastrium, nausea and vomiting, cold, clammy skin, marked fall in arterial blood pressure, tachycardia, distention of the neck veins and increase in venous pressure from 80 mm. of isotonic saline to 300 mm. The hematocrit rose from 38.1 per cent to 42.9 per cent and plasma albumin concentration from 2.90 Gm. per cent to 3.65 Gm. per cent, plasma globulin concentration from 2.55 Gm. per cent to 3.50 Gm. per cent, while the whole blood volume as deter-

mined by the radioactive phosphorus technic, fell from 4470 cc. to 4060 cc., the decrease being entirely in the plasma compartment, (within the error of the method) which decreased from 2760 cc. to 2280 cc. In this patient, therefore, not only did the 285 cc. of injected plasma disappear from the circulation, but also an additional 480 cc. of the original plasma volume. In five other patients we also observed an increase in the hematocrit following plasma infusion, even though some of them exhibited no clinical evidence of reaction. Freeman and Wallace[13] found similar clinical symptoms and signs as well as a rise in the venous hematocrit of unanesthetized dogs given four times concentrated serum rapidly (0.8 cc./kg./min.). Harkins, Boak and Brush[14] made the same observation in dogs following infusion of four times concentrated plasma, but did not find this to be true in a small number of splenectomized dogs. Brennan[7] noted an increase in the red blood cell count in acutely anemic neurosurgical patients following the injection of half normal plasma. Neither we nor any other investigators have observed similar findings of a decrease in plasma volume following the injection of purified albumin solution.

Proteinuria was not detected in any cases following the injection of either salt-poor human albumin or concentrated plasma.

From the data on plasma volume it was calculated that there was an average increase of 13.7 cc. per Gm. of albumin immediately following the injection of the 25 per cent solution. The comparable increase in plasma volume immediately following the injection of double strength plasma was 22.7 cc. This increase in plasma volume was greater immediately after infusion than at any other time in almost all cases.

In all but one of the patients with edema, a copious diuresis with weight loss and obvious diminution of edema occurred following the injection of the pure albumin solution. Red Cross plasma was not nearly as effective. (See Fig. 3.) Diuresis always occurred within 48 hours of the time of injection and was most marked in the first 24 hours. However, one patient with cirrhosis of the liver with ascites and minimal scrotal edema continued to gain weight and his ascites worsened, in spite of a very significant diuresis following two 50-Gm. injections of salt-poor albumin.

COMMENT

From the present observations it would seem justified to infer that a 25 per cent solution of salt-poor albumin is far superior to plasma in the treatment of chronic hypoalbuminemia of nutritional origin. This inference is based first on the bedside observations. Not only did the effect on diuresis seem better, but the pure albumin produced no pyrogenic reactions and no increases in venous pressure, in contrast to the effect of plasma.

The greater plasma-volume-increasing effect of plasma may be advantageous in acute conditions. In chronic states it would seem that this is less important than the concentration of albumin itself, which is increased more effectively by the pure albumin solution. By increasing colloidal osmotic pres-

sure, this should be more useful in nutritional edema and this was borne out by our bedside observations.

One may speculate as to the reason plasma volume is increased to a greater extent and over a longer period of time following the injection of plasma than after injection of an equivalent amount of albumin as salt-poor albumin (25 per cent). Some of the difference may be due to the greater volume of the plasma injected, but most is probably due to its greater sodium content, both as chloride and citrate. Further study with pure albumin diluted to the same concentration with or without added salt would probably answer this question.

Variations in the size of the red blood cells following infusion of concentrated human serum albumin solution seem to have received little notice. Metcalff,[25] using the same measurements we have used, demonstrated a decrease in the size of the red blood cells of dogs given concentrated serum as infusions. Harkins, Boak and Brush,[14] and Ashworth, Muirhead and Hill,[2] using the same indices, failed to demonstrate any change in the size of the dog's red blood cells following the injection of normal or hypertonic citrated or defibrinated plasma. Our findings in the human agree with the latter.

The disappearance from the circulation of injected albumin either as plasma or as concentrated albumin solution is of considerable interest and importance. Metcalff[25] concluded from studies on dogs receiving infusions of normal and concentrated serum or plasma that the rate of disappearance of protein from the circulation is logarithmic and therefore related to the total amount of protein in the circulation. Using labeled plasma protein in experimental animals, Schoenheimer et al indicated a "half-life" of plasma protein of about 14 days, whereas Bale and others, using similar technic, found that 50 per cent of the injected protein had disappeared from the circulation within 30 hours and 75 per cent within 6 days.[4] These authors did not find the rate of disappearance of injected protein to be logarithmic.

There is some suggestion from our data, as exemplified in Figure 5, that there is greater retention of albumin in the blood stream with successive injections given several days apart. There is no evidence that the albumin in the salt-poor albumin solution is any better in this respect than plasma. It may indicate that the extravascular sites become saturated on repeated injection. We have been unable to find any correlation between the severity of the malnutrition and hypoproteinemia and the retention of albumin in the circulation.

The initial plasma volume per kilogram of body weight noted in the present study was slightly lower than the average normal plasma volume reported in the literature and somewhat lower than the average normal plasma volume determined in this laboratory by means of the radioactive phosphorus method. The red cell volume and the whole blood volume were likewise lower. Two cases of cirrhosis of the liver had somewhat elevated plasma volume, the red cell volume being low and the whole blood volume normal or slightly elevated. This low value would be even more striking if the plasma volume, red cell volume and whole blood volume were calculated on the basis of the patient's

normal body weight before illness because all of these patients, even those in whom edema was present, had lost considerable weight. The decreased blood and plasma volume we found in patients with malnutrition and hypoproteinemia is in agreement with the results obtained by Walters, Rassiter and Lehmann[38] in repatriated prisoners of war. These authors used the dye method for the determination of plasma volume. With dietary treatment over several weeks they found the plasma and red cell volume to return to normal levels. On the other hand, Denz,[11] in a similar though less complete study, found the plasma volume to be increased in prisoners of war before treatment and to fall as their condition improved. Henschel et al[15] were in agreement with Denz. We found the plasma volume to increase with successive injections of both salt-poor albumin or concentrated plasma. There was no significant change in the red cell volume.

The figure calculated herein (13.7 cc.) for the increase in plasma volume per Gm. of injected albumin (as pure salt-poor albumin) is considerably lower than either the theoretical volume of 18 cc. per Gm.[31] or the values reported in previous clinical studies in man.[10, 17, 21, 22, 33, 34, 36, 37, 40, 43, 39] This discrepancy may well be explained by the fact that, unlike the method used herein, all of the clinical studies mentioned employed the dye method for determination of plasma volume. Use of the dye would be most likely to be misleading in patients in shock or patients with cirrhosis or nephritis. The larger figure calculated herein (22.7 cc.) for the increase in plasma volume per Gm. of albumin injected (as double strength plasma) may be due to the additional salt and protein present. Further studies would undoubtedly reveal the true explanation.

The effectiveness of salt-poor albumin in causing diuresis in cases of cirrhosis and nephrosis has been demonstrated by Thorn et al.[36, 37] It is likewise well known that plasma transfusions are much less effective in these patients and Leutscher[22] obtained little benefit from one injection of concentrated human albumin solution containing sodium chloride in patients with nephritis. We have found salt-poor human albumin to be much more effective than concentrated plasma in inducing diuresis with weight loss and relief of edema in patients receiving alternate injections of the two solutions containing equivalent amounts of albumin. The sodium content of the concentrated plasma may well explain this difference. That the sodium citrate may be responsible is indicated by the beneficial effect on nephrosis in children with injections of concentrated serum.[1]

The absence of untoward reactions following the injection of salt-poor human albumin is noteworthy, especially in contrast to frequency of reaction to concentrated Red Cross plasma. Homologous jaundice was not seen by us, but has been observed by others with plasma and must be counted as a disadvantage to the use of plasma not shared by pure albumin. Our observations on venous pressure, which usually increased significantly during plasma infusion and rarely during or immediately after albumin injection, must also be listed

as a mark of superiority of the latter over the former. This difference is probably due to the greater volume of fluid injected as well as its content of sodium chloride and citrate, which results in a greater increase in plasma volume.

The data presented herein have no bearing on the question of utilization of intravenously injected albumin. From the data obtained it is clear that albumin leaves the circulation just as rapidly when given as a salt-poor 25 per cent solution or as double strength plasma. Thus the metabolic behavior of the albumin in each case is probably the same. The superiority of the pure albumin in maintaining an elevated albumin concentration, therefore, is probably a temporary one, lasting for at least 24 hours. Our data gives no information in regard to its behavior after this period. Nevertheless, an effect lasting even for such a short period of time is of significance in the practical treatment of patients suffering a nutritional depletion of plasma albumin.

SUMMARY

1. Comparable injections of twice concentrated plasma and of 25 per cent salt-poor human albumin were studied in 22 patients with various diseases having in common malnutrition and hypoalbuminemia.

2. Both solutions caused an immediate and similar increase in albumin concentration, in total circulating albumin, and in plasma volume. However, significant differences were apparent within 24 hours. The concentration of albumin was more sustained with the solution of pure albumin than with plasma. This was due to the more sustained elevation of plasma volume produced by plasma. There was no significant difference in the increase of total circulating albumin following injection of either solution.

3. Pure albumin produced no increase in venous pressure whereas plasma did, particularly when a reaction occurred. No reactions occurred with albumin in contrast to their frequency with plasma.

4. There was no change in the size of the red blood cells following injection of either albumin or plasma.

5. The pure albumin solution was more effective than plasma in inducing diuresis with weight loss and relief of edema.

6. Solutions of 25 per cent salt-poor albumin would seem to be far superior to plasma in the treatment of nutritional hypoalbuminemia.

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STRANGULATED DIAPHRAGMATIC HERNIA *

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STRANGULATION HAS BEEN RECOGNIZED to be one of the most serious complications of the diaphragmatic hernia since Pare's[47] description of a case found at necropsy in 1564. Occasional cases of strangulated diaphragmatic hernia have been reported in the earlier literature, but prior to the widespread employment of roentgenography, the condition was seldom correctly diagnosed. In this paper strangulation is defined as the arrest of circulation due to compression. Compilation of reports from 1798 to the present reveals that the clinical picture follows a relatively stereotyped pattern which has not previously received adequate attention. In view of the fact that early surgical intervention alone can avert a fatal outcome, a discussion of this condition as a clinical and diagnostic entity seems warranted.

Our attention has been drawn to this condition by the observation of two cases within the past year, the first of which presented a clinical picture so atypical in our experience that a 24-hour delay before operation occurred, with subsequent death of the patient. Aroused by this incident to review the literature, we were able to collect 39 cases of strangulated diaphragmatic hernia and in all of them there was a strikingly repetitious symptomology. These cases are summarized here, together with four additional from the Cincinnati General Hospital (Table I).

Case 1.—A. G., colored male age 33, was admitted to the Cincinnati General Hospital April 13, 1947, with a history of cramp-like, non-radiating, epigastric and left upper quadrant pain for 23 hours. This pain was persistent, and had been accompanied in the ten hours previous to admission by vomiting of food without blood. From the time of onset there had been complete constipation. Two months previously he had been admitted to the surgical service with two stab wounds of the thorax; one a sucking wound of the right posterior thorax and the other in the left fifth interspace in the axillary line. There had been some doubt as to whether the latter had penetrated the pleura. A right hemopneumothorax developed after wound closure, but convalescence was otherwise uneventful, and he had returned to heavy labor.

Physical examination revealed a well nourished colored male who appeared acutely ill. Left diaphragmatic dullness could be percussed at the sixth interspace, and did not move on deep respiration. The abdomen was not distended; peristalsis was generally hypoactive. There was mild upper and left lower quadrant tenderness without spasm. No release tenderness was noted. There was an indefinite, vertically placed, fairly firm mass in the left lower abdomen, which was slightly tender and dull on percussion. Rectal examination was negative. Roentgenograms showed "high left diaphragm" and displacement of the heart to the right; films of the abdomen showed air in the large and small bowel with evidence of ileus (Fig. 1a). Barium enema revealed mesial and upward displacement of the sigmoid colon, but good filling and no evidence of obstruction (Fig. 1b). Transient "gurgling noises" in the left thorax were noticed by one observer. A diagnosis of left subphrenic abscess or delayed ruptured spleen was considered.

* Submitted for publication, April 1948.

TABLE I.—*Strangulated Diaphragmatic Herniae*

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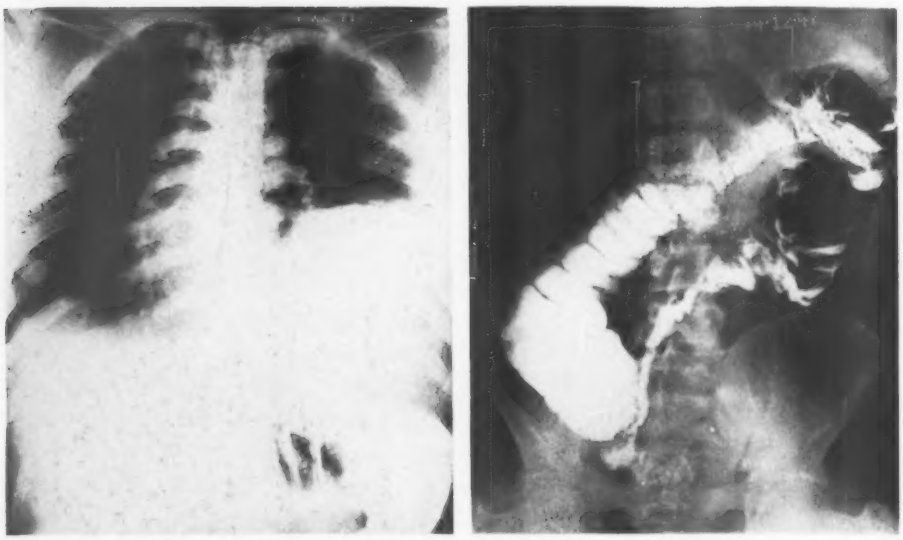
	Reporter and Date	Etiology	Type of Injury	Interval to Attack	Correctly Diagnosed	Hernial Contents	Operation Performed	Survival
(1)	Cooper 1798	congenit.	—	—	no	trans. colon, omentum	no	no
(2)	Boyle 1812	traumatic	stab	11 mos.	no	trans. colon, small intest., oment.	no	no
(3)	Greetham 1832	traumatic	stab	?	no	trans. colon, stomach, omentum	no	no
(4)	Reid 1840	traumatic	stab	15 mos.	no	trans. colon, omentum	no	no
(5)	Thompson 1847	traumatic	gsw	1 year	no	splenic flexure	no	no
(6)	Maiden 1869	traumatic	stab	1 year	no	splenic flexure, omentum	no	no
(7)	Hull 1874	traumatic	stab	1 year	no	transverse colon	no	no
(8)	Woodworth 1874	traumatic	indirect	10 days	no	small intestine, colon, omentum	no	no
(9)	Ord 1887	?	—	—	no	splenic flexure, omentum	no	no
(10)	Farwell 1888	traumatic	indirect	16 years	no	stomach, small intestine	no	no
(11)	McCloskey 1895	congenit.	—	—	no	stomach, sm. intest., spleen, colon, omentum	no	no
(12)	Mixter 1900	?	—	—	no	colon, omentum	yes	no
(13)	Home 1900	traumatic	gsw	4½ mos.	no	transverse colon, omentum	yes	no
(14)	Hawkes 1917	traumatic	stab	9 mos.	no	splenic flexure, small int., oment.	yes	yes
(15)	Symonds 1917	traumatic	gsw	?	yes	stomach, tr. colon, sm. int., oment.	yes	no
(16)	Warren 1919 I	traumatic	indirect	3 years	no	stomach, small intestine	yes	no
	II	traumatic	gsw	3 years	no	stomach, small intestine	yes	yes
	III	traumatic	gsw	?	yes	stomach, small intest., tr. colon	yes	no
(17)	Bryan 1921	traumatic	indirect	10 days	no	stomach, transverse colon, omentum	no	no
(18)	Waxman 1922	traumatic	gsw	2 years	no	splenic flexure	yes	no
(19)	Crook 1923	traumatic	stab	12 years	no	splenic flexure, tr. colon, oment.	yes	yes
(20)	Slater & McKenzie 1923	traumatic	gsw	4 years	no	stomach, transverse colon	yes	no
(21)	Stone 1923	congenit.	—	—	yes	splenic flexure	yes	yes
(22)	Ellis 1928	?	—	—	yes	transverse colon, omentum	yes	no
(23)	Gibson 1929 I	traumatic	stab	3 years	yes	colon	yes	yes
	II	traumatic	indirect	?	yes	stomach, transverse colon	no	no
	III	traumatic	indirect	1 day	yes	stomach	yes	yes
(24)	Russell 1930	traumatic	gsw	?	yes	stomach	yes	no
(25)	Johnson & Bowen (1932)	congenit.	—	—	yes	small intestine, ascending and transverse colon, omentum	yes	yes
(26)	Wright 1935	traumatic	indirect	?	no	stomach, spleen, omentum	yes	no
(27)	Mast and McDonough 1937	traumatic	gsw	8 mos.	yes	stomach and small intestine	no	no
(28)	Swinney 1942	traumatic	stab	6 weeks	yes	stomach	yes	yes
(29)	Deaner, McMenemy, Smith 1943	?	—	—	no	stomach and omentum	no	no
(30)	Jamieson 1943	traumatic	stab	1 year	yes	stomach and omentum	yes	yes
(31)	Gardiner	?	—	—	yes	stomach	yes	yes
(32)	Pfahl, Lund, 1944	traumatic	stab	18 mos.	no	transverse colon	no	no
(33)	Mackey, Bingham 1945 I	traumatic	gsw	6 mos.	no	splenic flexure, transverse colon	yes	no
	II	traumatic	gsw	3 years	yes	splenic flexure, transverse colon	cecostomy	no
	III	traumatic	gsw	6 mos.	yes	stomach and omentum	yes	yes
	Cases from the Cincinnati General Hospital							
G. H. 1933		traumatic	indirect	10 weeks	yes	transverse colon and omentum	yes	yes
E. L. 1945		traumatic	gsw	18 mos.	yes	transverse and descending colon, omentum	yes	yes
A. G. 1947		traumatic	stab	2 mos.	no	stomach, omentum	yes	no
W. H. 1947		traumatic	stab	7 years	yes	transverse and descending colon, omentum	yes	yes



A B

FIG. 1.—Case IA. Roentgenogram showing the heart displaced to the right and what appears to be a high left diaphragm, but actually is stomach herniated into the left thorax.

B. Roentgenogram following barium enema revealing satisfactory filling of the large bowel.

FIG. 2—Case I. Drawing illustrating conditions found at operation. Note the greatly dilated gangrenous stomach, filling a large portion of the left thorax. The original incision was a thoracic one in the eighth interspace, subsequently prolonged across the costal margin into the abdomen.

Several hours after admission he suddenly manifested signs of shock with peripheral circulatory collapse. At this time the left thorax had become dull to percussion up to the second interspace. Thoracentesis produced 550 cc. of fluid which resembled pure blood and had a RBC of 1.9 million.

Transfusion of 500 cc. of whole blood was followed by a rise in blood pressure. During the next few hours an additional 1,000 cc. of bloody fluid were removed from the left thorax. The following morning he manifested signs of increasing shock despite continuous blood transfusion. Repeat chest film showed increased mediastinal shift to

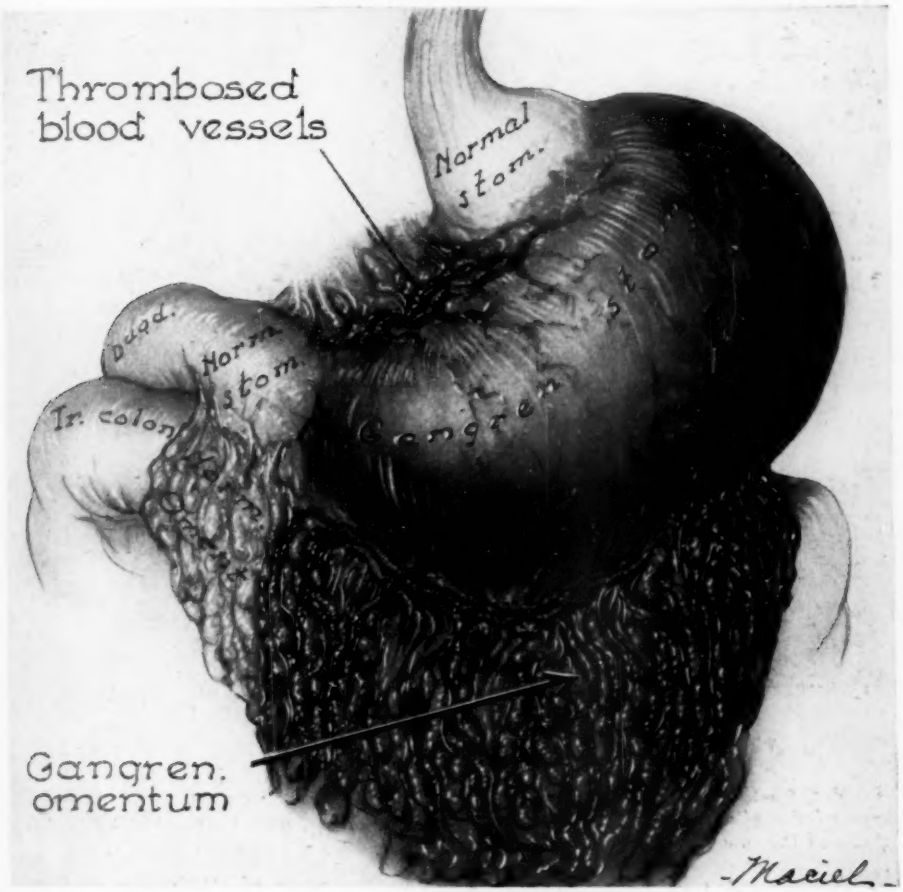


FIG. 3.—Case 1. The hernial orifice was so small that it precluded reduction of the stomach. Accordingly, the diaphragm was incised beginning at the costal margin and a clamp introduced through the hernial defect, in order that the remainder of the diaphragm could be safely divided, thus permitting adequate exposure of the stomach for reduction.

the right; unchanged position of the "high diaphragm," and increased amount of fluid in the left thorax.

At exploration, through a combined thoraco-abdominal incision, the stomach and spleen were found to be herniated through a rent in the diaphragm and the former to be entirely gangrenous save for a small segment of the greater curvature at the cardiac end (Fig. 2, 3). The entire omentum was gangrenous (Fig. 4). There was an estimated 1,000 cc. of bloody fluid in the pleural cavity. The gangrenous portion of the stomach

was resected and a post-colic Polya type gastro-jejunostomy was performed, only a small portion of the cardiac end of the stomach remaining as a pouch. The spleen and all of the omentum were removed.

Postoperatively there was evidence of improvement for 12 hours; however respirations became shallow and rapid, cyanosis could not be overcome by oxygenation or bronchial aspiration, and the patient expired 3 hours after operation.

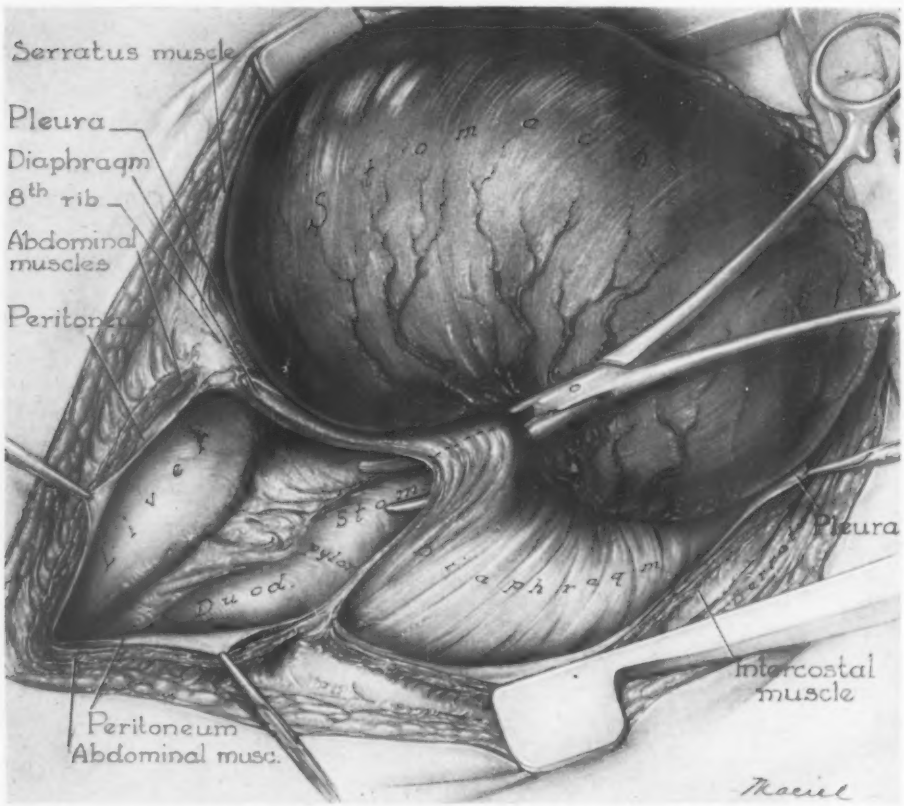


FIG. 4.—Case 1. Diagrammatic illustration indicating the extent of the gangrenous area of the stomach. Note the thrombosed vessels along both curvatures and the gangrene of the omentum.

An autopsy was performed and no immediate cause of death was discovered. There were 200 cc. of bloody fluid in the left thorax, the anastomosis was intact though there was a local area of gangrenous mucosa on the anterior wall of the stomach pouch, the heart appeared normal, and the lungs were crepitant. The mass in the lower left quadrant was a prolapsed kidney.

COMMENT

The correct diagnosis in the case was missed entirely and was not made until the thorax had been opened at operation. In retrospect the confusing features were: (1) the "high diaphragm" which was in reality the herniated stomach whose appearance on the roentgenogram accurately simulated that of an elevated diaphragm, (2) the absence of abdominal distention which was due to the stomach alone, unaccompanied by intestine, being herniated through

the rent in the diaphragm, (3) the presence of very bloody fluid in the left chest. The features which should have suggested the proper diagnosis were: the history of a penetrating wound in the lower left thorax, the marked vomiting not productive of bile-stained fluid, the dislocation of the heart to the right, and the dullness in the left lower thorax.

Diaphragmatic herniae have been classified by Astley Cooper[1] into three categories: (1) Congenital: due to defects in the diaphragm arising from faulty embryologic development, (2) acquired: which develop at points of anatomic weakness, e.g. at the esophageal hiatus, aortic, or caval openings, and (3) traumatic; caused by rents in the diaphargm arising from direct or indirect trauma.

Strangulation is infrequent in both congenital and acquired diaphragmatic herniae. Cooper[1] in 1798 described a case of the former, noting: "When the congenital opening of the diaphragm is small, consequences are not immediately fatal. It produces some inconveniences which increase in the progress of life and at length destroys as in other herniae by a strangulation of protruded parts." Usually, however, the congenital defect is large and consequently admits ingress and egress of large portions of coelemic organs without serious constriction. In our series of 43 cases with strangulation only four were congenital, and 34 were traumatic.

Traumatic diaphragmatic hernia constitute over 90 per cent of cases complicated by strangulation, and for this reason we have particularly directed our attention toward this type. From an etiologic viewpoint this type of hernia falls into three main classifications, (1) those caused by stab wounds of the thorax, (2) those caused by gunshot wounds of the thorax, and (3) those caused by indirect violence to the diaphragm, such as falls, compression injuries, and steering wheel accidents.

Traumatic diaphragmatic hernia showed an increased incidence during and immediately after the first world war, and will undoubtedly show a similar tendency following the recent conflict. Wounds of the diaphragm are not prone to heal, and many observers believe that upon severance of the diaphragm negative pressure in the thorax causes ascent of intra-abdominal organs through the new orifice. A portion of omentum plugs the opening and at the same time separates the muscle fibers, preventing their subsequent union. The opening is thus maintained as a constant mortal threat to the patient. Thirty-four of the cases in the present study were traumatic in origin, the initial factor being stab wounds in 38.2 per cent, gunshot wounds in 38.2 per cent, and indirect trauma in 23.5 per cent. Five cases of the total group were of undetermined etiology, and four were congenital.

SYMPTOMS

Premonitory symptoms referable to the abdomen or thorax were noted prior to the acute attack in 30.2 per cent of the total group. All but one patient with premonitory symptoms gave a history of previous trauma. Typical symp-

toms included sporadic pain, usually located in the left thorax or left upper quadrant of the abdomen; less commonly, flatulence, constipation, and vomiting were noted; and still less frequently, dyspnea and cyanosis occurred.

The interval between the initial injury and the acute attack can be extremely variable, as short as one day or as long as 16 years. In 85 per cent of the cases, however, strangulation occurred within three years after injury.

The acute attack usually begins abruptly; in 29 instances the attack was definitely stated to have been sudden in onset. In 85 per cent of the traumatic cases, relatively sudden increase in the intra-abdominal pressure was noted as a precipitant of the acute attack. Eating or drinking was cited in 9 cases, physical stress in 8, and straining at stool in one.

Pain, vomiting, constipation, dyspnea, and hiccoughing are symptoms commonly noted during the acute attack. Pain, characteristically sudden, has been the most usual initiating symptom. Specifically mentioned in 37 instances, pain was noted in various locations, and often in a combination of anatomic areas. In 44 per cent of the cases there was pain in the left upper quadrant; in 30 per cent in the left thorax; in 16 per cent in the epigastrium; in 7 per cent in the right lower quadrant; in 10 per cent around the umbilicus; and in 27 per cent there was generalized abdominal pain. Most characteristically the pain has been located in the upper portion of the abdomen, and has frequently been associated with pain in the inferior portion of the left thorax. It is commonly severe and colicky, and may prostrate the patient. Although many writers have stressed radiation of pain into the left shoulder, it was found in only 11 per cent of the 43 reported cases.

Vomiting was specifically mentioned as occurring in 88 per cent of the cases, usually simultaneous with, or soon after, the onset of pain. In some instances it was the initial complaint. In cases in which the stomach has been strangulated, vomiting is early, protracted, and ineffectual, frequently with evidence of blood.

Although the incidence of hiccough has been relatively infrequent, having been found in 4 cases, or 10 per cent of the total, its presence is important as being suggestive of diaphragmatic irritation.

Constipation was mentioned specifically in 21 instances in this series, or a total of 49 per cent of the cases. It frequently preceded the onset of the acute attack and probably represents a precipitating factor since it likely caused increased abdominal pressure and thus sponsored the tendency for strangulation. When it manifests itself during the acute attack it is associated with other signs of acute intestinal obstruction such as abdominal distention, hyperactive peristalsis, and the inability to pass flatus or feces. It is well to emphasize that these symptoms during the acute episode are similar to those associated with obstructions of the colon. Although constipation has been associated with strangulation of the stomach, in such instances it generally precedes the attack and is not complete. Thus the effectual movement of the bowels, the presence of an undistended abdomen, and normal peristaltic intes-

tinal activity have presented serious confusion to the observer in those instances in which the stomach alone is strangulated. The obvious signs of acute obstruction are most prominent when the obstruction is located in the intestinal tract; they are not nearly so emphatic in cases of obstruction at the stomach.

Dyspnea was mentioned in 15 or 35 per cent of the cases. Appearance of this symptom depends largely on the suddenness and the degree of encroachment by the herniated portions and the accumulated fluid upon the cardiorespiratory system.

PHYSICAL FINDINGS

The diagnosis of diaphragmatic hernia was always a matter of extreme difficulty prior to the advent of roentgenology. Bowditch[4] in 1853 collected 88 cases of diaphragmatic hernia available in the literature to that time and presented one case of his own. His own and one other were the only cases diagnosed before autopsy up to that time. With roentgenology a formible method of establishing diagnosis has been acquired. It should be emphasized, however, that in strangulated diaphragmatic hernia at least one or more abnormal physical signs are present in the thorax which should direct attention to this part of the body. Gibson[13] in 1930 reported three cases of strangulated diaphragmatic hernia which he diagnosed clinically without aid of roentgenology. He stressed the importance of the clinical signs in such cases, and the necessity of appreciating them, in view of the fact that many of these patients were so acutely ill as to prevent necessary roentgenologic examination. In one of our cases the correct diagnosis was considered, but roentgenologic confirmation could not be obtained because of the patient's precarius condition. Gibson stressed the following diagnostic symptoms: (1) Diminished expansion of the chest, (2) impairment of resonance, (3) adventitious sounds, (4) cardiac displacement, (5) circulatory collapse, (6) cyanosis and dyspnea, and (7) asymmetry of hypochondria.

Physical findings in the abdomen are in no way diagnostic. Attention is generally focused on the abdomen because of the presence of pain in some region, which as such is usually misleading. As pointed out, the pain is usually located in the upper portions of the abdomen and there is associated tenderness to palpation in those areas. As with other types of intestinal obstruction, when the obstruction is low the pain is very apt to be generalized, the abdomen may be distended, and other evidences of intestinal obstruction may be present. If the stomach is obstructed, the abdomen may be scaphoid and in other respects quite normal in appeareance. Some observers have placed importance on unusual concavity of the left hypochondrium representing the area voided by migration of abdominal viscera into the thorax. This finding is apparently quite rare, and did not occur in any of our cases.

The greatest emphasis must be placed upon physical examination of the chest. Records given in the literature of examination of the chest have been somewhat incomplete. Physical examination was recorded in 30 of the 43 cases analyzed. In 27, or 90 per cent of these, at least one of the following was

present: (1) Dullness in the left thorax, found in 18, or 60 per cent of the cases; (2) cardiac shift, found in 14 cases, or 47 per cent; (3) tympany of the left thorax, occurring in 13 cases, or 40 per cent; adventitious sounds (gurgling, tinkling, or peristaltic sounds in the thorax), found in six cases, or 20 per cent; and (5) succussion splash, found in two cases, or 6 per cent.

Fluid has been found in the thorax either on physical examination, at operation, or at autopsy in 12 of the 43 cases (30 per cent). The character of the fluid was described in nine of these, *and in eight was noted to be bloody or sero-sanguinous.* This is a point of special interest, since in one of our cases and in two other cases—one reported by Deaner, McMenemey, and Smith[29] in 1943, and another by Pfahl and Lund[32] in 1944—the diagnosis was confused by the bloody fluid in the thorax and the failure to recognize that as much as 3½ liters may be found in conjunction with strangulated diaphragmatic hernia. This fluid may closely resemble blood and in one case a RBC count of 1.9 millions per cc. was noted. Deaner, McMenemey, and Smith were the first to point out the possible occurrence of sero-sanguinous effusion with strangulation, but its presence in the thorax has been noted at necropsy in reports as far back as Astley Cooper. This clinical finding deserves special significance. It unquestionably occurs more often than has been reported and should occur in all cases of strangulated diaphragmatic hernia except those of short duration, since the pathologic physiology differs in no way from strangulation in other types of herniae where bloody fluid is commonly seen.

Roentgenograms were made in 21 cases, with correct diagnosis in 16. As far as roentgenologic examination is concerned, the points which were found to be important are: (1) The simulation by the herniated viscus of high diaphragm. In a case with radiologic evidence of an apparently high diaphragm and an accompanying history of previous thoracic injury, the patient should be considered a candidate for diaphragmatic hernia until proven otherwise. (2) Cardiac shift to the right is almost always present and is noteworthy. Physicians may be apt to rationalize cardiac shift on the basis of high diaphragm or by the presence of what appears to be fluid in the left thorax. Cardiac shift does not normally accompany elevated diaphragm and is not apt to be present unless there are large amounts of fluid or viscera in the thorax. (3) In many instances the presence of air bubble above the normally anticipated level of the diaphragm establishes diagnosis immediately. This gas bubble need not appear, however, and the presence of a homogenous density below a somewhat convex border presumed to be diaphragm may be misleading. In one instance (Case 1) the stomach was herniated above the diaphragm, the superior border of the stomach simulated the arch of the diaphragm, and there was no air in the stomach. The diagnosis of diaphragmatic hernia was thought to be impossible. (4) Patients often show roentgenologic evidence of fluid in the thorax.

The transverse colon is the portion of the gastro-intestinal tract which most frequently herniates into the thorax. Tabulation reveals that the herniated organs were as follows: transverse colon, 23 times, or 53.4 per cent;

stomach, 20 times, or 45 per cent; small intestine, 11 times, or 25 per cent; splenic flexure, 10 times, or 23 per cent; descending colon, five times, or 11.5 per cent; colon (site undesignated), four times; spleen, twice; and ascending colon, once. The most frequent occurrences were: stomach alone, eight times; transverse colon alone, seven times; splenic flexure alone, seven times; stomach and transverse colon, four times; stomach and small intestine, four times; and splenic flexure and transverse colon, three times.

It becomes quite clear from a perusal and statistical analysis of the case histories that in traumatic diaphragmatic hernia, which comprise the greatest percentage of those cases which become strangulated, a singularly common pattern of events ensues and presents a rather typical picture. The patient is commonly a male previously in good health. Review of his past history will reveal a traumatic episode involving the thorax either by a stab or gunshot wound in the region of the diaphragm or by a severe contusion. He is seized suddenly with acute pain generally located in the upper abdomen, most frequently in the left upper quadrant, and associated with pain in the lower portion of the left thorax. A cardinal symptom, radiation of pain to the left shoulder, is sometimes present, and directs attention to the diaphragm immediately. Characteristically the pain is precipitated while eating, drinking, or exercising. Almost simultaneously with the onset of the pain, the patient begins to vomit and continues to do so without relief. Thereafter he develops signs of acute high or low bowel obstruction, depending on the viscus involved. Physical examination will reveal one or more signs directed to the left thorax. Usually dullness or tympany of the left thorax is present inferiorly with concomitant suppression of breath sounds. In a great number of cases there is cardiac shift to the right. Occasionally extraneous bowel sounds in the chest, in themselves pathognomonic of hernia, are detected. Aspiration of the left thorax based upon physical signs will reveal bloody fluid. Roentgenologic examination will frequently reveal cardiac shift to the right and one of the following findings: (1) a recognizable portion of the gastro-intenstinal tract in the left thorax above the diaphragm, most frequently a loop of large intestine, (2) an apparently very high left diaphragm, (3) fluid in the left thorax.

To recapitulate, the following should suggest the diagnosis of strangulated diaphragmatic hernia: (1) signs of acute gastro-intestinal obstruction, (2) history of an old injury, (3) physical findings referable to the left thorax, particularly cardiac shift to the right and, on occasions, bloody fluid on aspiration, and (4) roentgenologic evidence of a high left diaphragm.

TREATMENT

It may seem trite to emphasize that the treatment of strangulated diaphragmatic hernia is emergency surgery. Hedblom[36] pointed out in 1925 that when obstruction develops the mortality is doubled. In 126 collected cases with acute intestinal obstruction he found the mortality to be 53.1 per cent.

In our collected series of 39 cases of strangulated diaphragmatic hernia, the mortality for the period 1798 to 1919 was 88.8 per cent, with an operative

mortality rate of 66 per cent. For the period 1920 to 1945 the general mortality rate was 57.1 per cent and the operative mortality 43.7 per cent. In our own series of four cases, the mortality rate was 25 per cent.

The senior author emphasized in 1935 the advisability of utilizing the transthoracic route for the attack on diaphragmatic hernia.[34] Such an approach is especially suited for small hernia since it allows the operator to investigate the diaphragm under excellent visual conditions. When there is no strangulation of the viscera the incision is adequate for the reduction of the organs and successful repair of the hernia. When a large amount of viscera has been strangulated the thoracic incision should be extended across the costal margin into the abdomen. Opportunity to inspect the strangulated abdominal organs is afforded, and the operator can understand the pathology of viscera below the diaphragm as well as utilize the previously mentioned advantages of better exposure and easier reduction of the hernia afforded by the thoracic approach. We believe that the combined thoraco-abdominal approach should be considered in all cases of strangulated diaphragmatic hernia but that the initial incision should be made thoracically rather than abdominally, and the extension across the costal margin into the abdomen made when the exact circumstances have been appraised from above. The reasons for the thoracico-abdominal approach have been emphasized by Carter,[35] who cites the conclusive advantakes: (1) excellent exposure is provided, (2) the herniated viscera are often adherent to the lung, the thoracic wall, or the diaphragmatic ring, and must be freed from above under direct vision, (3) access to the diaphragmatic orifice is easily gained, (4) when tears are located near the heart, sutures can be placed accurately and with less danger of wounding the heart, the esophagus, and the mediastinal vessels than might occur with an abdominal incision alone.

CASE REPORTS

Case 2. (Previously reported by B. N. Carter[34]).—G.H., colored female age 45, was admitted to the Cincinnati General Hospital on October 1, 1933, complaining of cramp-like pains in the abdomen. Ten weeks before admission she had fallen from a third story window and suffered a central dislocation of her left hip. She was a patient in the Cincinnati General Hospital at that time for seven weeks. During her first hospital stay there were no symptoms referable to the abdomen or to the thorax but physical examination on discharge from the hospital revealed some dullness at the left base of the chest. Two days before the second hospital admission the patient began to have cramp-like pains in the abdomen immediately after eating a large plate of pork and beans. These pains occurred particularly in the upper right quadrant and in the lower left thorax. *The pain was referred sharply to the shoulder and somewhat into the left neck.* There was a sensation of suffocation and palpitation. The patient had vomited almost everything she had eaten the previous day and there had been obstinate constipation for two days.

Physical examination showed a thin, gray haired negress who was suffering acute cramp-like pains and was screaming with agony. Examination of the thorax disclosed dullness and flatness in the lower left portion. Auscultation showed striking peristaltic noises in the thorax which could be heard without the aid of a stethoscope. The abdomen was slightly rounded and tense. No peristaltic patterns could be seen although a great many peristaltic sounds were heard over the abdomen. A diagnosis of dia-

phragmatic hernia with intestinal obstruction was made. This was confirmed by roentgenologic examination with the patient in a sitting position. The outline of the large bowel could be seen in the lower left thorax without the aid of opaque material.

The patient was operated upon immediately. A high mid-line incision was made in the epigastrium, and dilated large bowel was seen which disappeared through a defect in the diaphragm. Some of the large bowel was reduced through the opening into the abdomen but complete reduction could not be effected until the opening in the diaphragm had been enlarged by a lateral incision. Nine inches of colon were found in the thorax. The bowel was dark red in color and there were about 150 cc. of blood-tinged fluid in the left pleural cavity. The opening in the diaphragm was immediately anterior to the esophagus. The edges of the ring were indurated and fibrotic, indicating that the hernia had been present for some time. There was no sac present. The rent in the diaphragm was closed with double medium silk sutures and the abdomen was closed in the usual way. Convalescence was uneventful. Subsequent roentgenograms have shown the hernia to be cured.

COMMENT

The diagnosis in this case was suggested by the pain referred to the left shoulder and was confirmed by the presence of pathognomonic peristaltic sounds in the left thorax and by roentgenologic examination which, without the aid of barium, revealed a dilated loop of bowel above the diaphragm. The circulation in the involved bowel was impaired, as evidenced by the dusky red color and a small amount of bloody pleural fluid. In this instance the diaphragm had been ruptured by indirect violence.

Case 3.—E.L., white male age 26, was admitted to the surgical service on December 26, 1944. One week earlier he had been seen in the receiving ward of the Cincinnati General Hospital complaining of sharp sudden lower abdominal pain of knife-like character, associated with nausea and vomiting. A diagnosis of gastroenteritis was made and he was referred to his local physician. For the enusing seven days he was bedfast at home, suffering with severe abdominal pain which became more generalized and then moved to the left flank and the left costovertebral angle. During that time he vomited frequently, had no bowel movements, and did not pass any flatus. Past history revealed that he had been admitted to the Cincinnati General Hospital for a penetrating gunshot wound of the thorax on March 15, 1943, at which time it was thought likely that the bullet had traversed both lungs and had probably perforated the lower end of the esophagus. While in the hospital he developed a bilateral hemothorax, pericarditis without effusion, and on his 14th hospital day had a sudden internal hemorrhage manifested by several tarry stools. He recovered with conservative therapy and was discharged on April 13, 1943.

Physical examination revealed an acutely ill male, temperature 100.4, blood pressure 96/70. A healed gunshot wound in the mid-axillary line at the level of the 6th rib, and another on the posterior aspect of the right thorax were found. Percussion note was hyporesonant over the left base posteriorly. Breathing was grunting in character. The heart was not enlarged to percussion and sounds were distant and weak, with rhythm being regular. The abdomen was moderately distended with slight voluntary spasm chiefly on the left side, and was absolutely quiet. No masses or organs were felt. Laboratory tests revealed the following: WBC, 12,400; hemoglobin, 13.5 Gms.; urine, negative; serum chlorides, 340. A flat film of the abdomen showed many dilated loops of small bowel with multiple fluid levels. Diagnosis of intra-abdominal abscess with resultant ileus and obstruction was made.

On December 27, 1944 he was noted to have signs of fluid in the left thorax. Thoracentesis was performed and 150 cc. of foul smelling *serosanguinous* fluid were with-

drawn. This fluid had a specific gravity of 1.020, and on smear was found to contain gram positive cocci and gram negative rods. Diagnosis of strangulated diaphragmatic hernia with empyema formation was made. Roentgenologic examination of the thorax revealed marked displacement of the heart to the right and congestion in the left lung field. Barium enema showed the colon to be normal as far as the splenic flexure, where there was an annular constriction 2-3 cm. in length through which a very small amount of barium passed.

Because of the patient's poor condition, cecostomy and closed thoracostomy were immediately performed, followed on January 3, 1945 by a Devine colostomy, and repair of the hernia by the thoracic route on February 27, 1945. On May 1, 1945 the colostomy was resected with end-to-end anastomosis. Postoperative course throughout these procedures was stormy, and the patient signed out against advice on May 14, 1945.

COMMENT

This case presents several interesting features. It exemplifies one possible development if a strangulated hernia is allowed to progress unrecognized and if the perforation of the bowel occurs into the thoracic cavity. In such cases empyema develops and it is probable that certain of these cases have been treated for their pleural disease without recognition of the underlying pathology. Such a case was reported by Slater and McKenzie[20] in 1923. Their patient was operated upon for intestinal obstruction of undetermined cause located at the splenic flexure. Because of the patient's poor condition, a cecostomy was performed, following which he did well but developed purulent fluid in the left chest. A rib resection was done, the pleural cavity drained, and the patient recovered. He was re-admitted to the hospital eight months later with severe abdominal crampy pain, vomiting, hiccough, and dullness of the left lower lobe. He subsequently died, and autopsy revealed herniation of the transverse colon and the cardiac end of the stomach through a rent in the diaphragm.

Our case illustrates a similar method of treatment in such instances; that is, a cecostomy for decompressing the bowel plus local drainage at the site of strangulation. The repair of the hernia can then be undertaken from the thoracic route at some future date when the patient is in suitable condition.

The correct diagnosis was not immediately arrived at in this instance though there were present a history of penetrating wound of the chest in the region of the left diaphragm, signs of intestinal obstruction, physical findings referable to the lower left thorax, and displacement of the heart to the right. Only after bloody foul smelling fluid had been aspirated from the thorax was the proper diagnosis suspected and confirmed by barium enema.

Case 4.—W. H., colored male, age 35, was seen in the receiving ward of the Cincinnati General Hospital on May 31, 1947 by a medical consultant. His illness began suddenly 6 days previously when, following an alcoholic debauch, he was seized with acute agonizing pain in the epigastrium with radiation into the left thorax and into both shoulders. He immediately vomited and continued to do so on the days following. He was severely constipated and passed no feces or flatus except for two or three lumps of hard stool after an enema. Past history revealed he had suffered a skull fracture in 1920 and a stab wound of the left lower chest in 1939.

Physical examination revealed a sweating, orthopneic, dyspneic colored male. Temperature was 100.2; blood pressure, 130/90; pulse, 120; respirations, 40. Dullness to flatness was noted on percussion over the left lower thorax and absent to diminished breath sounds were noted in the same area. A stab wound scar was present over the 7th rib in the left anterior axillary line. The abdomen was diffusely distended. There was voluntary muscle spasm but no localizing tenderness. No peristalsis could be heard.

Clinical diagnosis was left lower lobe pneumonia with paralytic ileus on the basis of the pneumonia. A chest film was secured and revealed what was thought to be a high left diaphragm. The diagnosis of a probable subphrenic abscess was now entertained and surgical consultation was requested. The tentative diagnosis of strangulated diaphragmatic hernia was made on the basis of the medical consultant's report, and upon examination of the patient these confirmatory findings were elicited: The left thorax was noted to be dull posteriorly as previously described and, in addition, the lower portion anteriorly was decidedly tympanitic; the apex beat of the heart was noted to be in the fourth interspace to the right of the sternum; review of the chest film revealed that the heart and mediastinal structures were shifted to the right, a homogeneous density containing an area of radiolucency was seen to occupy the lower half of the lung field, and the left diaphragm could not be identified; flat and erect films of the abdomen showed the pattern of large bowel obstruction, and gas was noted to be present in the large bowel as far distally as the splenic flexure; upon barium enema the bowel could be filled only up to the splenic flexure.

Operation was performed immediately by a combined thoracico-abdominal incision. A portion of the transverse colon and the splenic flexure had herniated into the thorax through an opening in the anterior half of the left diaphragm that would accommodate only two fingers. Approximately 600 cc. of non-odorous bloody fluid were found in the pleural cavity. The 10-inch segment of herniated colon was severely dilated and purple in appearance. Upon reduction its color improved noticeably but there was a 4 cm. area of bowel which retained a mottled black appearance and was of questionable viability. The strangulated bowel was reduced into the abdomen after the opening in the diaphragm had been greatly enlarged. The thoracic portion of the wound was closed after the diaphragm had been repaired. The questionable loop of bowel was exteriorized as a double barreled colostomy and the abdominal wound closed with silver wire. In addition, a cecostomy was performed. His postoperative course was very satisfactory. On the third postoperative day his wound was dressed and it was discovered that the segment of bowel in question had actually been non-viable and was now completely gangrenous. This portion of the bowel was resected without anaesthesia being required. He was maintained on penicillin and sulfadiazine therapy. Clinical signs of fluid developed in the left thorax on the 15th postoperative day and a thoracentesis was performed on the 17th day with the removal of 1000 cc. of straw-colored fluid which was negative on culture. His course thereafter was afebrile, and on July 7, 1947 the colostomy was closed by side-to-side anastomosis. He was re-admitted on October 27, 1947 and the cecostomy was closed on October 30.

This case illustrates the ease with which diagnosis can be made in these cases when one is cognizant of the signs and symptoms of strangulated diaphragmatic hernia. Case 1 had been so striking and so recent that the similarity with this case could be noted even in the history. The diagnosis was readily made in view of the history of previous penetrating wound of the left lower thorax, the signs of intestinal obstruction, the displacement of the heart, the roentgenologic findings suggesting a high diaphragm on the left, and the signs of fluid in the left chest. No thoracentesis was performed, but at operation there were 600 cc. of very bloody fluid in the thorax. A combined incision

was made on account of the hugely distended loop of colon which occupied a large part of the left pleural cavity and which could not be reduced through the exposure afforded by either a thoracic or an abdominal approach.

SUMMARY

In a review of 39 cases from the literature together with four cases from our own hospital records, the clinical picture of strangulated diaphragmatic hernia is presented. Emphasis is placed on the striking consistency of the history and physical findings as follows: (1) history of a previous thoracic injury, (2) physical findings referable to the left chest, particularly displacement of the heart to the right, dullness or tympany in the lower portion of the thorax, adventitious sounds, and aspiration of bloody fluid from the left pleural cavity, (3) roentgenologic findings suggestive of a high left diaphragm with displacement of the heart to the right, and (4) signs of acute gastrointestinal obstruction with particular emphasis on the fact that where the stomach alone is strangulated there is absence of abdominal distention and a patent intestinal tract.

The use of a combined thoracico-abdominal incision is recommended in the surgical treatment.

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RECONSTRUCTION OF THE EXTERNAL EAR*†

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RECONSTRUCTION OF THE EXTERNAL EAR to correct for substance lost by reason of congenital, post-infectious, or posttraumatic defects, or following excision of malignant tumor, represents one of the most difficult problems in plastic surgery. An abnormal ear is conspicuous and an absent one is a major cephalic deformity. Criteria for successful reconstruction have been set down by Suraci who lists seven points as essentials if the reconstruction is to be acceptable to patient and to surgeon. These are: correct size, similarity of outline, similarity of height, correct cephalo-auricular angle, permanency of size and shape, rigidity of the ear and matching color. The earliest attempts at reconstruction of the ear fell far short of this goal.

Survey of the literature reveals that Tagliacozzi,[2] in the 16th century, referred to the repair of partial losses of the ear by the use of flaps of skin from the scalp or neck. Also, Dieffenbach,[3] in 1830, outlined the reconstruction of partial defects by the use of local flaps. In 1870, Szymanowski[4] reported his technic for subtotal reconstruction of the external ear. The method utilized the principle of the local flap, outlined in butterfly shape on the scalp, then elevated and folded on itself. In 1907, Nelaton and Ombredanne[5] proposed a local flap for partial loss of the ear, providing rigidity by the insertion of a free graft of cartilage. Gillies[6] (1920) embedded free grafts of cartilage in the auricular area, elevating the constructed pinna into position at a second operation. Van Dijk[7] (1926) reported one case of total loss of the ear following a burn by electricity. He used a compound cervico-thoracic flap incorporating costal cartilage. De River[8] (1927) utilized the Szymanowski "butterfly" flap combined with a tubed pedicle. Graham[9] (1927) used septal cartilage as a buried transplant, reflecting a flap of skin from behind the ear at the second stage of the procedure. Graham also reported a case of Pierce[10] in which buried costal cartilage had been elevated and backed with a stent graft of skin after which a thoracic tubed pedicle was transplanted to simulate the helix of the ear. Pierce[10] (1930) reported four cases in which he used free cartilage as an inlay graft combined with a cervical tubed pedicle to construct the helix. Lockwood[11] (1930) reported two cases constructed by the use of pedicled flaps of soft tissue. The results were not comparable to those of Pierce. New[12] (1931) published photographs of one case of partial traumatic loss repaired by a tubed flap from the thoracic area. Easer[13] (1935) used foreign material, hard rubber, to supply rigidity to the reconstructed ear. Padgett[14] (1938) reported four cases in which he had used Pierce's technic modified

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by the use of a split flap of soft tissue. Newman[15] (1941) reported two cases in which Pierce's technic had been used with gratifying results. Gillies[16] (1937) reported on his failure in one case to make use successfully of a pedicled flap supported by carved grafts of iliac bone. He also listed cases in which

FIG. 1.—The technic of cutting free cartilage grafts by gouge as shown at the left causes compression of the cartilage so that some degree of distortion or curling of the graft is unavoidable. The use of two scalpels as shown at the right prevents abnormal compression of the cells and minimizes the tendency to curling.

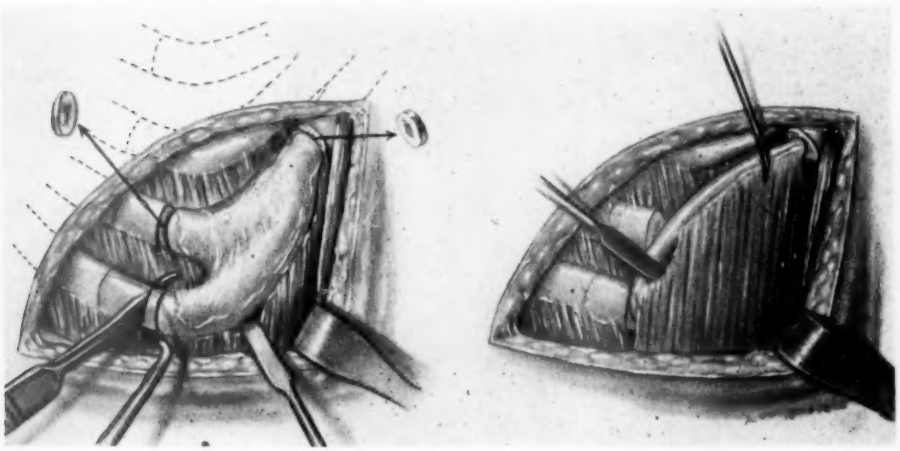

FIG 2.—Sketch showing the technic of cutting the costo-chondral cartilages so that a large free graft may be obtained from the site of fusion of two cartilages. The excision of a disc, 2 to 3 mm. in thickness, at the level of each transection facilitates the removal of a large block of cartilage.

cartilage from the maternal ear was substituted as a homoplastic graft for the absent auricle. This type of transplant was successful in five of seven cases. Nattinger[17] (1937) also reported two cases in which maternal ear cartilage had been used successfully. Pierce and O'Connor[18] (1938) used preserved cartilage from cadavers or living cartilage from the ear of the mother. Kirk-

ham[19] (1940) also reported on the use of cadaver cartilage for reconstruction of the ear. In his technic the dead cartilage was perforated freely and soaked in solution of formalin to establish rigidity of the graft. A further report by Gillies[20] (1941) listed 16 cases in which cartilage from the mother's ear had

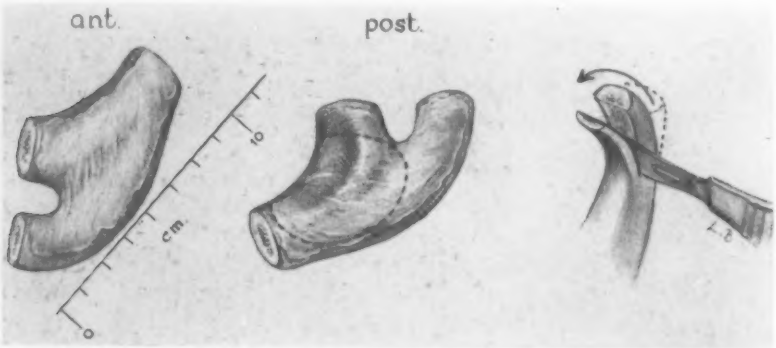

FIG. 3.—Sketch showing the anterior and posterior aspects of a specimen of costochondral plate at the level of fusion of the cartilages of the 8th and 9th ribs. The posterior aspect of such a specimen is concave. As the costal cartilage is thinned by carving, advantage is taken of the tendency of such cartilage to curl, in order to exaggerate this concavity. The transplant is embedded under the skin of the auricular region in such a way that the concavity of the graft assumes the position of the concha of the normal ear.

FIG. 4.—Case 1 (a) congenital microtia corrected by use of a cervical tubed pedicle. (b) pedicle detached at its lower end and sutured to upper portion of pinna. (c) appearance after suture of the tubed pedicle to the ear.

been transplanted to the child; 11 of these were considered successes. In two cases there was aseptic absorption of the cartilage and in three the grafts were lost due to sepsis. Greeley[21] (1941) used this method but later reported that there was absorption of the maternal cartilage. Young[22] (1940), in animal experimentation, observed that strips of costal cartilage healed by cartilaginous union when transplanted to articular surfaces. Then, in 1941, Young[23] pre-

sented a new idea. In animal experiments he determined that autogenous costal cartilage, finely chopped and seeded over the fascia of the rectus muscle, stayed viable and fused into a solid sheet of opaque "cartilage-like" tissue. The fused areas were found to consist of fibrous tissue. Grossly this tissue had some of the properties of fibro-elastic cartilage. Peer[24] (1943) reported on the

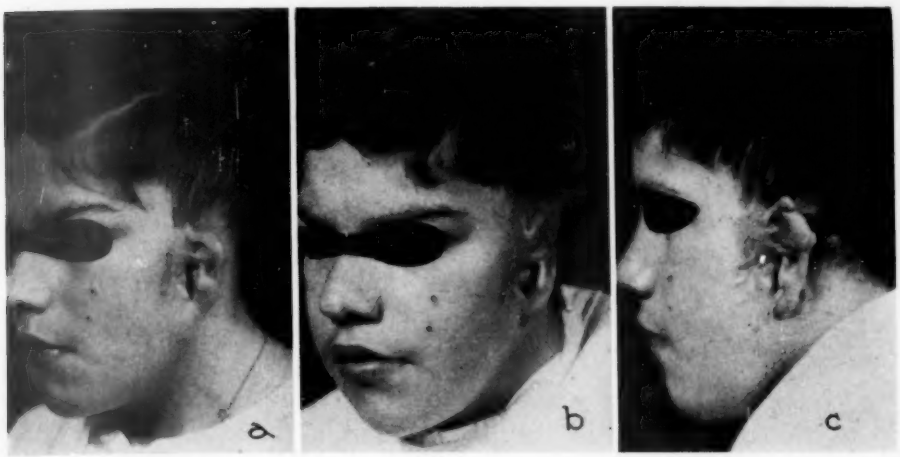

FIG. 5.—Case 2 (a) Congenital microtia. (b) Appearance after implantation of carved costal cartilage. (c) After elevation of cartilage graft and backing with a split graft of skin. Further revision of the tissue of the helix is necessary in this case.

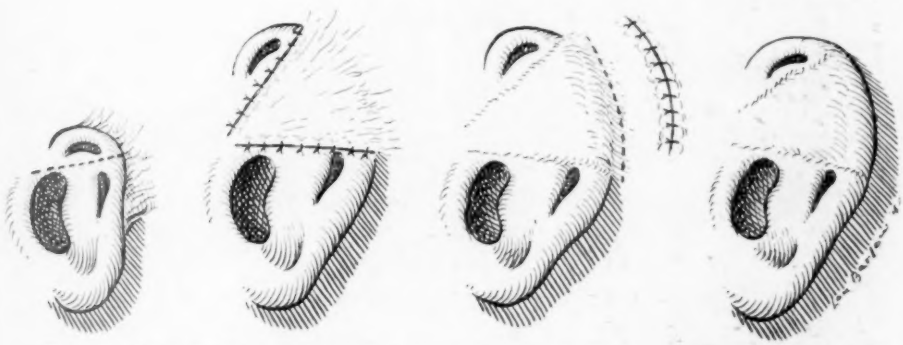

FIG. 5.—(d) Sketch of operative steps involving the transverse section of the rudimentary ear, rotation of the superior and inferior portions and their suture to the skin of the post-auricular area, the implantation of a carved graft of costal cartilage and the elevation of the graft from the head and its backing with split skin graft.

use of finely chopped pieces of cartilage as grafts in the reconstruction of the external ear in humans. He referred to such finely chopped costal cartilages as "diced cartilage grafts." In 1943 he[25] reported on the accurate formation of such fibro- cartilage into the shape of auricular cartilage by the use of a perforated bi-valved mold of vitallium which had been filled with "diced" cartilage and buried in the abdominal wall for three months. This fibro-cartilaginous

framework was then successfully transplanted beneath the skin of the aural area. Young[26] (1944), using a perforated mold of ticonium, cast fibro-cartilaginous grafts in the shape of the auricular cartilage. He reported one case

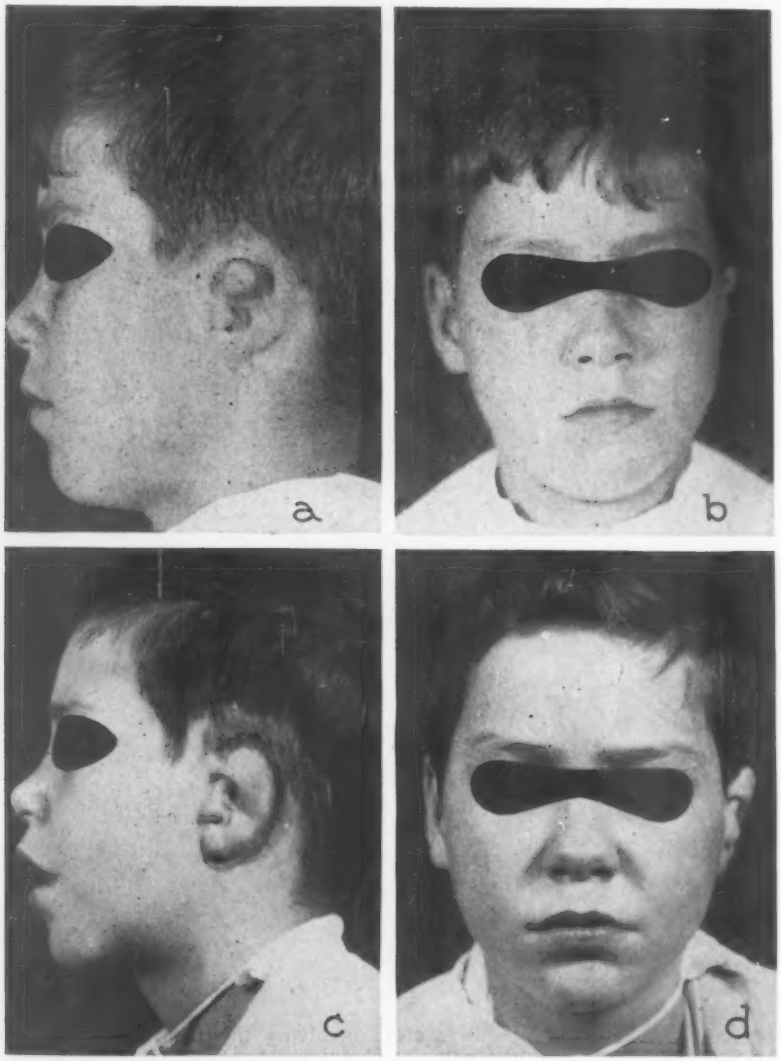

FIG. 6.—Case 3 (a and b), Congenital absence of the ear. (c and d), Appearance after reconstruction by use of a carved graft of cartilage and its elevation and backing with a split skin graft.

in which the principle was applied to the construction of the external ear. Aufricht[27] (1947) reported on the pre-casting of auricular cartilage by the use of a perforated acrylic mold, filled with flat chips and thin platelets of cartilage and buried in the abdominal wall. He emphasized the necessity for the use of a generous flap from the scalp in the creation of the concha, recognizing that

the pressure of a tight cutaneous flap tends to obliterate the contours of auricular cartilage which have been constructed by this method. This experience of Brown et al[28] (1947) in reconstruction of the ear indicated that suitable reconstruction of the external ear can be accomplished by the use of carved costal cartilages. They emphasized that reconstructive surgery of this magnitude need not be prolonged but can be accomplished in cases of loss of helix or pinna in only two stages and that total reconstruction of the ear can be completed in three operative stages.

FIG. 7.—Case 4 (a). Congenital absence of the ear. (b) Appearance after implantation of large, carved graft of costal cartilage. (c) Appearance after elevation of cartilage and application of split graft of skin behind the ear. Reconstruction in two stages.

During the past two years the authors have had experience with ten cases of reconstruction of the external ear. These were managed on the Surgical Service of The New York Hospital and on the Plastic Surgery Service of the U. S. Veterans' Hospital,* Bronx, New York. The general principles of the technic of Pierce have been followed with agreement in execution with the advancements of Brown et al. In several cases subtotal reconstruction of the ear has been carried out in two stages. The authors have had no experience with molded cartilage grafts. The management of cases included in this report has led to the opinion that suitable reconstruction of the external ear can be accomplished if sufficient attention is given to the cutting and the carving of costal cartilage, to the importance of the establishment of a lateral concavity to represent a concha, and to the many minor details which enter into the execution of this type of reconstructive surgery.

CARVING OF COSTAL CARTILAGE

Experience in the handling of fresh costal cartilage has led to observations which have contributed to success in obtaining a suitable restoration of the

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external ear. A common objection to the use of straight grafts of cartilage in reconstructive surgery is that, after transplantation, the graft may undergo distortion of shape, curling. Figure 1 shows the technic of cutting grafts from

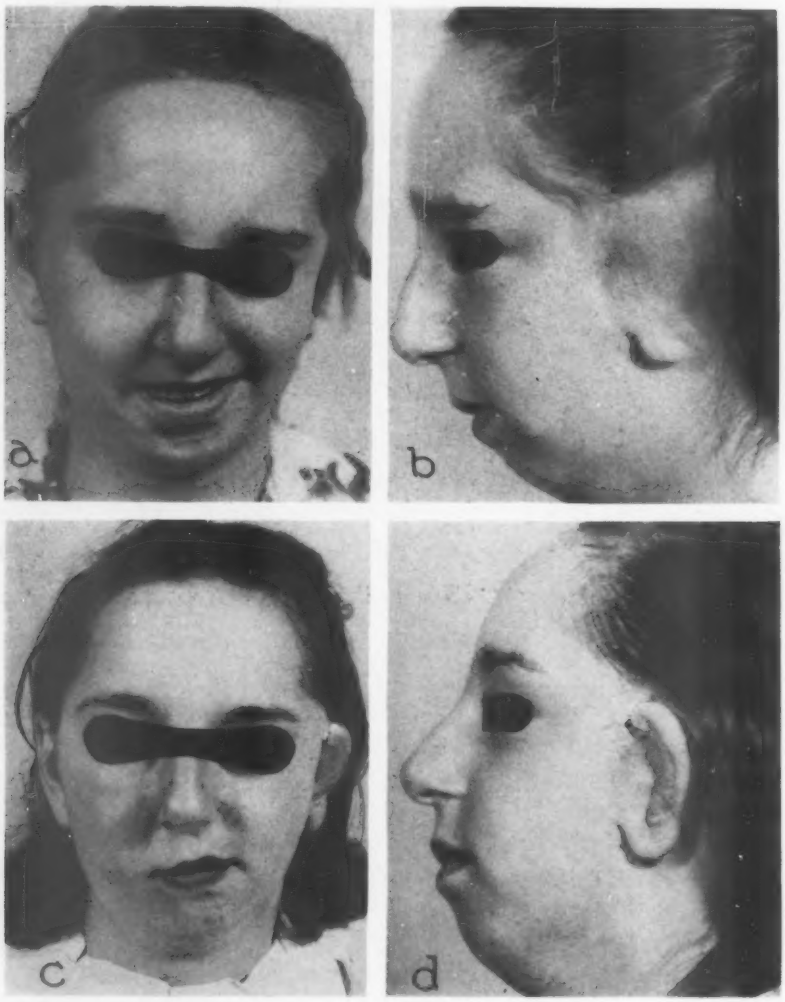

FIG. 8.—Case 5 (a and b) Congenital absence of the ear in association with facial asymmetry. (c and d) Appearance after reconstruction by implantation of carved costal cartilage, elevation of the cartilage and backing with a split skin graft and use of a tubed pedicle to simulate the appearance of the helix.

costal cartilage by gouge and by scalpel. The use of a gouge causes compression of medullary and cortical cells of the costal cartilage in such a way that, even after carving, the graft tends to warp or curl. The use of two scalpels as shown prevents abnormal compression of cells and minimizes this tendency. On microscopic examination of the transversely cut edge of costal cartilage it

is apparent that the center of the cartilage is yellow and the periphery is grey. The gross structure of the costal cartilage is somewhat similar to that of bone. It is stated in Gray's[29] "Anatomy" that "in the thickest parts of the costal cartilages a few large vascular channels may be detected. This appears, at first sight only, to be an exception to the statement that cartilage is a non-vascular tissue; actually the vessels give no branches to the cartilage substance itself, and the channels may rather be looked upon as involutions of the perichondrium." This gross structure apparently causes a variation in tissue tension when the costochondral cartilage is cut or carved. Figure 2 shows the approach to the costochondral plate commonly used in securing a graft. In order to obtain a large graft two adjacent rib cartilages are resected en bloc. The

FIG. 9.—Case 6 (a) Squamous cell carcinoma of the ear. (b) Appearance after primary excision of tumor and suture of ear to the post-auricular skin. Following this step a patterned framework of tantalum mesh was inserted under the skin in the region of the aural defect. (c) After elevation of post-auricular skin and tantalum mesh and application of a skin graft to the post-auricular wound.

excision of a disc, 2 to 3 mm. in thickness, at the level of each transection makes easier the removal of such a block of cartilage. Inspection of such a graft from its posterior aspect shows (Fig. 3) that there is a concavity in the cartilaginous portion of the thoracic cage. This can be used effectively in the carving of cartilage for reconstruction of the ear. As the rib cartilage is split longitudinally, advantage is taken of the curling effect to exaggerate this concavity. Cartilaginous or fibro-muscular fusion of two adjacent cartilages is made use of in obtaining the desired width of graft. With attention to these details, it is possible to cut and carve, from costochondral cartilage, a free graft which has size, shape and rigidity, suitable for reconstruction of the external ear.

CASE REPORTS

Case 1. ***Partial congenital absence of the external ear.*** In this case as shown in Figure 4a, b, c, the microtia was corrected by the use of a cervical tubed pedicle. Reconstruction was carried out in three stages: the construction of the tubed pedicle of skin in the neck, the transfer of its distal end to the upper, anterior margin of the pinna, and the final division of the tubed pedicle with suture to the outer margin of the ear.

Case 2. *Partial congenital absence of the external ear.* In this case the operative steps were carried out as shown in Figure 5d. Transverse section of the rudimentary ear at the junction of its middle and upper thirds with rotation of the upper third anteriorly and suture of both segments to the skin of the mastoid area was done at the first operation. A free graft of carved cartilage was inserted as a wedge at the second operation. Elevation

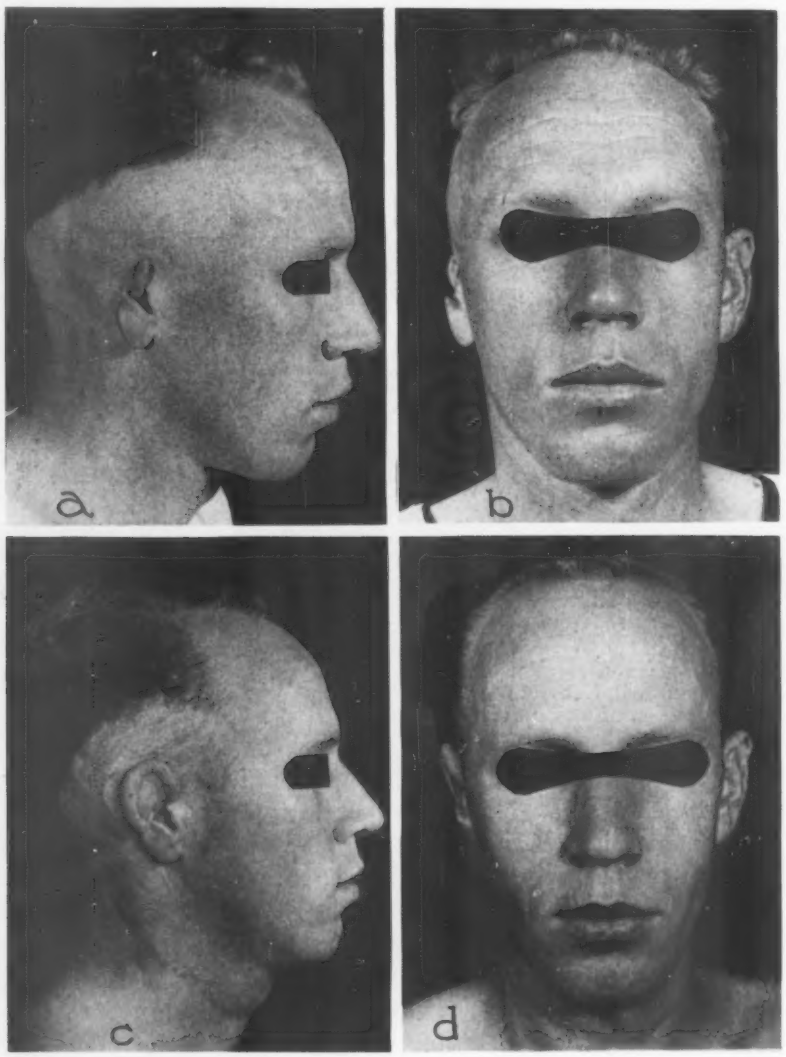

FIG. 10.—Case 7 (a and b) Traumatic loss of upper two-thirds of ear. (c and d) Appearance after reconstruction by use of carved cartilage and tubed pedicle from neck.

of the graft and backing with a split skin graft was done at the third operation. Minor revision of the tissue in the region of the helix is required before this reconstruction can be looked upon as completed. Photographs are shown in Figure 5 a, b, c.

Case 3. *Congenital absence of the external ear.* In this case (Fig. 6) the position of the rudiment of the ear was such that it was necessary to carve a graft from costal

cartilage in the shape of the letter "C." This was embedded at the first operation. At the second step the cartilage was elevated from the head and a split skin graft was applied behind it. At a third operation the congenital remnant of ear cartilage was displaced behind the graft. This increased the lateral concavity to simulate a concha, provided rigidity to the constructed auricle and established the proper cephalo-auricular angle.

Case 4. *Congenital absence of the external ear.* In this case (Fig. 7) the small rudimentary ear was used only as a foundation for the reconstruction. Carved costal cartilage

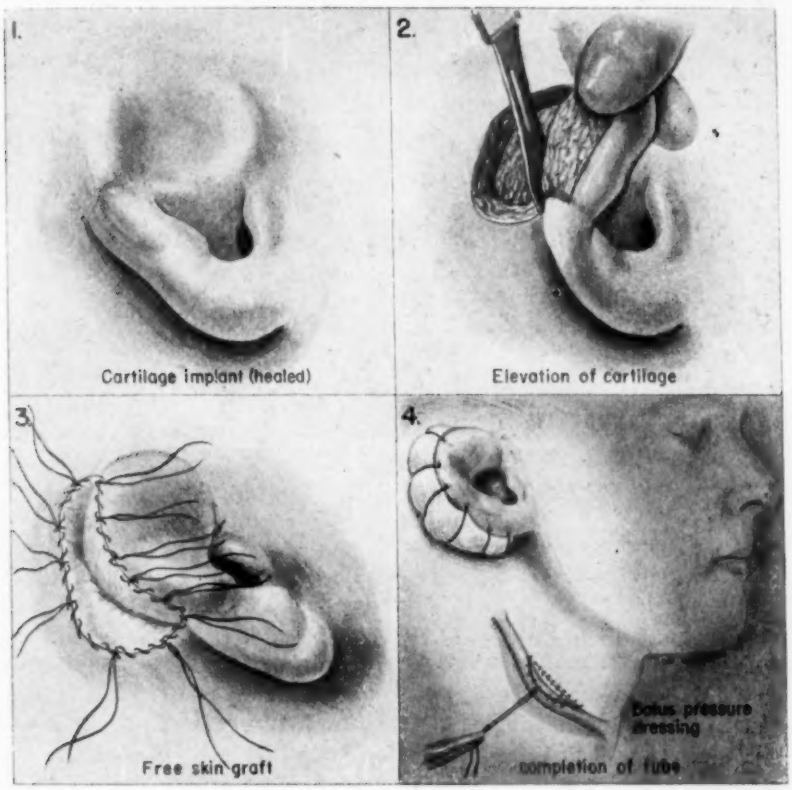

FIG. 10.—(e) Steps in elevation of implanted cartilage, backing with split skin graft and construction of tubed pedicle.

was buried in the auricular area at the first operation. At the second operation the cartilage was elevated from the head and a split skin graft was applied to the posterior aspect of the graft and to the defect of the aural and mastoid regions. Reconstruction was completed in two stages.

Case 5. *Congenital absence of the external ear.* Operative steps one and two in this case were the same as in Cases 3 and 4. The curling of the cartilage in this case was used to maximum effect in the simulation of the concha. (Fig. 8.) The associated facial asymmetry made the estimation of the required size of graft difficult to determine. Rather than disfigure the skin of the cervical region in this young girl, a tubed pedicle was constructed on the arm and transplanted to the ear in the reconstruction of the helix. This construction required three additional operative steps, five operations in all.

Case 6. *Loss of substance of the middle third of the ear by the surgical excision of malignant tumor.* This patient had a squamous cell carcinoma of the skin of the ear which

nad invaded the auricular cartilage. At the time of excision the remainder of the ear was sutured to the post-auricular skin as shown in Figure 9. At the second operation a supporting framework of tantalum mesh was inserted under the post-auricular skin now in the middle third of the ear. At the third operation the constructed ear was elevated from the head and a split skin graft applied behind it.

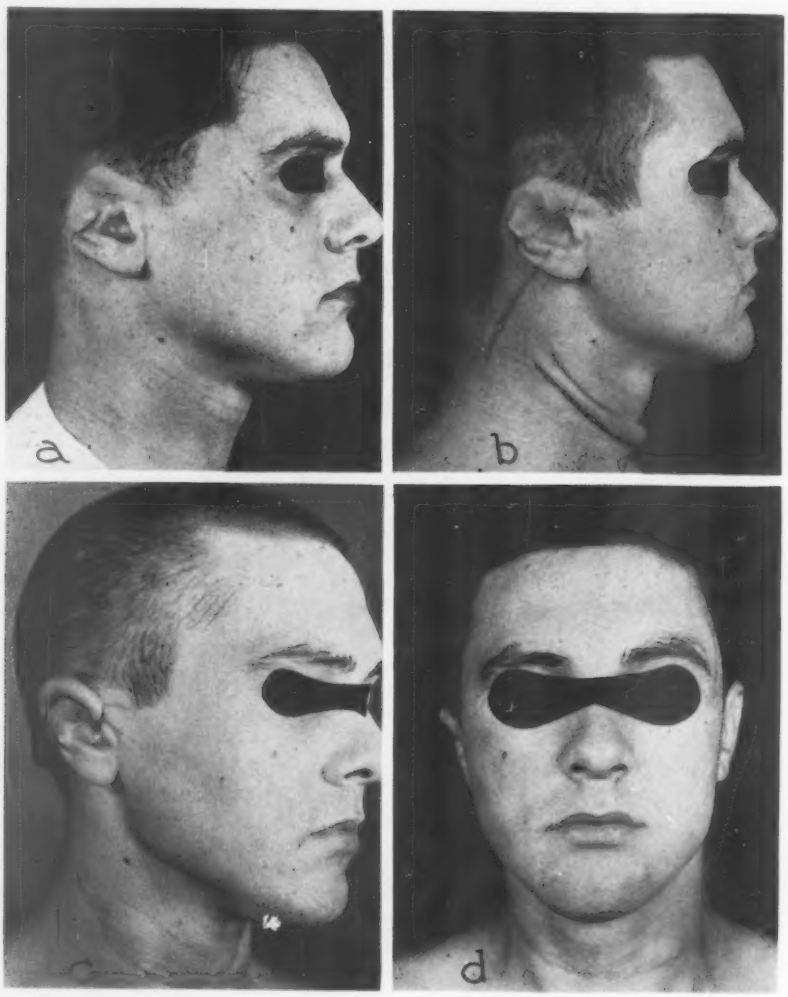

FIG. 11.—Case 8 (a) Traumatic loss of upper half of ear. (b) Appearance after implantation of carved cartilage. (c) Appearance after elevation of cartilage graft and application of a tubed pedicle to simulate the helix. (d) Front view after reconstruction.

Case 7. *Traumatic loss of upper two-thirds of external ear.* The patient lost the upper two-thirds of his ear in an injury in which he was thrown from a jeep. The ear was amputated by flying glass. Photographs are shown in Figure 10. Reconstruction was by the insertion of carved cartilage, its elevation and application of a skin graft posteriorly and the use of a cervical tubed pedicle to construct the helix. Visible defect

of the scalp in the region of the cephalic portion of the skin graft was camouflaged by tattooing.

Case 8. *Traumatic loss of upper half of external ear.* This patient lost the upper half of his ear in an automobile accident. Photographs are shown in Figure 11. Reconstruction was carried out five years after the primary injury. Operative steps were the same as in Case 7.

Case 9. *Traumatic loss of upper half of external ear; reconstruction by recovery and implantation of autogenous auricular cartilage.* In an accident in which this patient was thrown from an automobile the upper half of the ear was amputated. The astute interest of a resident surgeon sent the relatives to another hospital where first aid treatment had

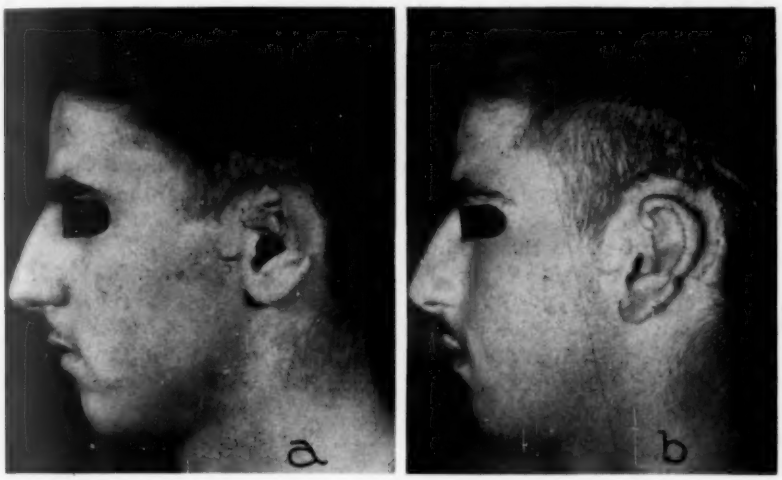

FIG. 12.—Case 9 (a) Traumatic loss of upper half of ear. (b) Appearance after reconstruction by use of autogenous auricular cartilage (see case report) and reproduction of appearance of helix by revision of soft tissue over the cartilage graft.

been given. The amputated ear was recovered from a basin of discarded dressings. It was washed with soap and water, sterilized with merthiolate solution. The skin was then removed and the auricular cartilage was buried in the abdominal wall. The lacerated ear was sutured to the skin of the mastoid area. Six weeks later the cartilage was removed and implanted behind the post-auricular skin. It was disappointing to note the excessive fibrosis around the cartilage. At subsequent operations the cartilage has been elevated from the head. Photographs are shown in Figure 12.

Case 10. *Congenital absence of the external ear.* In this case particular difficulty was encountered because the anomally left only skin of the scalp in the aural region. After implantation of a large carved graft of cartilage there was excessive growth of scalp hair over the skin of the new ear. A tubed pedicle was used to construct the helix. Displaced hair of the scalp was removed by electrolysis.

SUMMARY

Ten cases are reported in which partial or complete reconstruction of the external ear has been carried out. Reconstructions have been effected by the use of buried free grafts of cartilage, their elevation from the head and their backing by free grafts of skin at a second operation. A small tubed pedicle

has been used to effect the appearance of the helix in some cases. Technical details in the cutting and carving of costal cartilages have been set down. The opinion is advanced that reconstruction of the external ear, acceptable to patient and to surgeon, can be effected if attention is given to these details.

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CHOLEDOCHUS CYST *

Case Report with Brief Comment

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THE GREAT RARITY of the condition known as choledochus cyst or idiopathic cystic dilatation of the common bile duct as judged by the paucity of reports in the literature, should make the report of a single case diagnosed preoperatively and successfully treated by primary anastomosis to the intestinal tract of some interest. Its relative infrequency is manifested by the fact that Judd and Greene[5] at the Mayo Clinic were able to find only one case despite a review of 17,381 biliary tract operations covering a period of 19 years. Likewise, Smith[12] at the Presbyterian Hospital in New York, collected only two choledochus cysts from 757,000 admissions to that institution. Numerous excellent reviews of the literature pertaining to this condition are to be found, notably those of McWhorter[8] in 1924, Zinninger and Cash[14] in 1932, and, more recently, of Shallow *et al.*[11] in 1943. The latter group were able to collect only 175 cases, and Smith could find only 181 cases in the literature. McLaughlin[7] is of the opinion that the total number is certainly less than 200. According to Blocker *et. al.*,[2] Lavenson credited Vater in 1723 with finding the first choledochus cyst. Clark[4] remarks that the first case report was made by Todd in 1817, and Saint[10] states that Neugebauer, in 1924, was the first to diagnose a case preoperatively. Since that time diagnosis still remains uncommon. Berkley[1] reported a diagnostic error of 98% in reviewing 53 cases. Many authors, particularly Zininger and Cash,[14] Morley[9] and Ladd and Gross,[6] feel that the high mortality associated with this condition results primarily from failure to recognize the true pathologic condition either preoperatively or at the time of surgery, and therefore failure to institute or an undue delay in instituting anastomosis between the intestine and the biliary tract. The etiology of this condition remains obscure, although many hypotheses have been advanced, practically all of them dealing with some developmental anomaly either of formation or of growth.[9, 11, 14]

CASE REPORT

E.R.S., Hospital No. 123963, 5-year-old white male, was first admitted to the Surgical Service of the Beckley Hospital on May 7, 1947, with the major complaints, as given by his mother, of intermittent abdominal pain, occasional slight jaundice, alcoholic stools, abdominal mass, low-grade fever, and episodes of nausea and vomiting, these symptoms having repeatedly occurred with increasing intensity since the age of two years.

History of Present Illness and Previous Admissions.—According to the mother, the patient was the fourth of five normally born children, and the first two years of his life had been quite uneventful. At the age of three, however, he began to complain occasionally of right upper quadrant pain, this being noticed most often following the ingestion of food. The pain was described as being cramplike, doubling the child up during the more severe episodes. At about the same time the mother observed that his skin and

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sclera were frequently yellow. The symptoms described above became more marked, and at about the age of four a mass was discovered in the right upper quadrant for the first time. The mother stated that the mass fluctuated considerably in size from day to day. Alcholic stools began to be noticed, usually occurring following episodes of fever associated with enlargement of the mass and the appearance of jaundice. These symptoms continued, and he was first hospitalized on the Pediatric Service of this institution on May 13, 1946, when the abdomen was found to be distended and there was a large palpable mass in the right upper quadrant, the latter being interpreted as an enlarged gallbladder. His temperature was 100.4 on admission. Laboratory studies revealed a fragility test with no increase in hemolysis, an icterus index of 53, and a red blood count of 3.9 million with a hemoglobin of 56% (photoelectric); the white blood count was normal; the van den Bergh test showed a reaction of the immediate obstructive type; and urinalysis was negative except for a biliuria. A flat roentgen-ray film of the abdomen revealed what was thought to be a large mass in the right upper quadrant. A cholecystogram failed to reveal any gallbladder shadow, leading to the roentgenographic diagnosis of a probable pathologic gallbladder. On conservative therapy the jaundice declined and the fever subsided; and as these improved, his abdominal complaints disappeared. In view of his improvement the patient was discharged from the hospital, a diagnosis of acute catarrahal jaundice having been made.

Following discharge from the hospital, he was asymptomatic for approximately four weeks and then again began to have the same type of attacks. His mother noticed that the mass apparently was becoming larger very gradually and tended always to be present to some extent, even between acute episodes. On April 29, 1947, he was readmitted on the Pedriatic Service for further study. At that time his temperature was 100.6, and he was clinically slightly icteric. A mass was present in the right upper quadrant, somewhat larger than on the previous admission and this time was interpreted as an enlarged liver. The mass was slightly tender on palpation. On this admission the icterus index was 23, and again the van den Bergh reaction was of the immediate obstructive type; urinalysis was negative; stool examination revealed no bile; red blood count was 4.36 million with a hemoglobin of 81% and a color index of .94; there was a leukocytosis of 15,500 with an essentially normal differential count. Again on symptomatic treatment he became afebrile and the mass in the right upper quadrant receded somewhat. He was discharged, a diagnosis of acute hepatitis having been made. He was readmitted to the hospital on the Surgical Service one week later for further investigation.

Past Medical History. Not remarkable.

Previous Operations. Uneventful tonsillectomy and adenoidectomy in October, 1946.

Family History. Irrelevant except for the fact that a paternal uncle died at the age of nine, reputedly with "yellow jaundice and gallstones."

Physical Examination:

General Appearance. On this admission the child was well nourished and well developed with a definite icteric tinge to the skin and the sclera. Temperature, 99.

Head, eye, ear, nose and throat. Negative.

Lungs. Clear to palpation, percussion and ausculation.

Heart. No arrhythmia, murmurs or enlargement were detected.

Abdomen. The superficial veins of the abdomen, as well as of the lower chest, were unusually prominent. The abdomen was slightly distended. A very large mass could be felt and seen in the upper abdomen extending approximately three fingerbreadths below the costal margin on the right and extending down somewhat less on the left. Beneath this mass on the right a second tumefaction could be felt extending well below the umbilicus and out into the right flank. The upper, larger mass was firm, moderately tender, and

was interpreted as liver. The lower mass had a cystic consistency and could be moved slightly, particularly in the transverse axis. The spleen was not palpable. Normal peristaltic sounds were heard on auscultation of the abdomen. No spasm or rebound tenderness were present. The costovertebral angles were negative.

Rectal Examiantion. Negative.

Remainder of physical examination negative.

Laboratory Findings:

Blood. Red blood count, 4 million with a hemoglobin of 80%; serology on two occasions, negative; clotting time, 4 min. 25 sec.; bleeding time, 1 min.; reticulocyte count, 1.5%; prothrombin time, normal.

Blood Chemistry. Admission icterus index, 35; urea nitrogen, 7 mg.%; fragility test revealed hemolysis beginning in a dilution of .34% and incomplete in a dilution of .26%; cephalin flocculation test, negative.

Urinalysis. Negative except for ++++ biliuria.

Stool Examination. Negative for bile.

Roentgen-ray Findings:

Chest and Abdomen. Flat film of the abdomen showed a great increase in density of the right upper and mid-abdomen. The lower half of the right kidney was outlined and was apparently of normal size, shape and position. From this film a roentgen-ray diagnosis of a large mass of the right upper and mid-abdomen was made. Roentgen-ray examination of the chest was negative.

Intravenous Pyelogram. No abnormalities of the urinary tract were visualized.

Gastro-intestinal Series. This showed marked displacement anteriorly and to the left of the first and second portions of the duodenum, apparently by a large extrinsic mass. Fourth-hour examination showed downward and medial displacement of the first portion of the transverse colon.

Preoperative Course in the Hospital.—The patient's temperature varied considerably during this period of observation, there almost always being slight fever, but recordings as high as 101 were made on several occasions. He was treated with glucose infusion, as well as a high-caloric, high-carbohydrate, and high-protein diet and was given large amounts of vitamin K daily. The low-grade jaundice varied considerably from day to day but subsided gradually, and the patient was icterus-free by the time surgery was performed. Episodes of severe abdominal pain occurred frequently, causing the child to cry bitterly. These attacks occurred most often immediately after meals. The cystic mass was found to change in size as much as 3-4 centimeters from day to day, a general regression in size occurring as his icterus subsided. Coincident with his general improvement and the decrease in icterus, one got the unmistakable impression that the mass had become much smaller.

A diagnosis of choledochus cyst was made and the patient prepared for laparotomy.

Operation.—Exploratory laparotomy; aspiration and biopsy of choledochus cyst; biopsy of liver; choledochocystoduodenostomy. (May 17, 1947.)

Anesthesia. Ether.

The abdomen was opened through a mid right-rectus incision. Upon opening the abdomen, the lower mass described previously was found to consist of a large, yellowish-tinged, tense, spherical, cystic structure covered with a veil-like layer of posterior peritoneum (see Figure 1). Just above this and extending bilaterally across the abdomen well beneath the costal margins, the diffusely enlarged liver could be seen, this apparently representing the firmer upper mass palpated preoperatively. The liver was of normal color but was somewhat granular in appearance. Jutting out from beneath the right margin of the liver and wedged between it and the cystic mass beneath was an extremely large, tense, thick-walled gallbladder, the latter appearing to be on top of the cyst. The duodenum had been greatly displaced and distorted and, instead of being in the usual

position, was actually extremely anterior and to the left of the midline. It was greatly flattened out and ribbonlike, being drawn tightly over the anteromedial aspect of the cyst and conforming to the contour of the latter. The pylorus was quite far anterior and was also displaced somewhat to the left. The right transverse colon had been displaced downward and the hepatic flexure, downward and mesially. Although fairly well fixed,

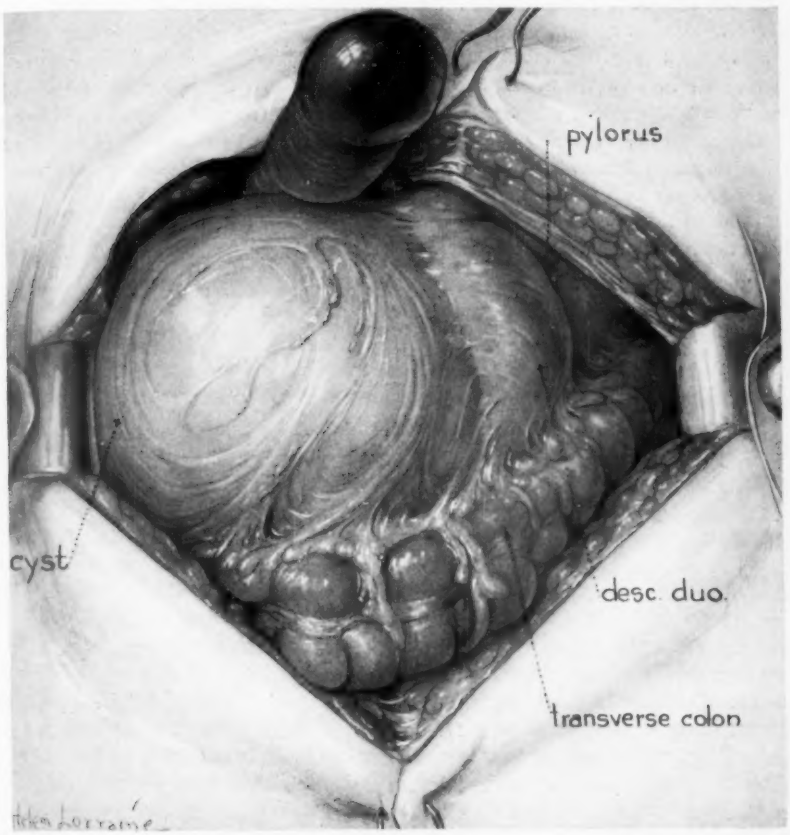

FIG. 1.—Artists' conception of the operative findings. The liver edge and the tense gallbladder can be seen beneath the right costal margin. The displacement of the transverse colon is also noted, as well as the marked anteromedial displacement of the duodenum and the pylorus.

the mass was found to be moderately movable in a transverse axis. The cystic duct was slightly enlarged in caliber and was found to empty into an apparently normal common hepatic duct just above the origin of the cystic mass. The common duct distal to the cyst appeared to be slightly enlarged on palpation but was otherwise negative. A number of soft hyperplastic lymph nodes were discovered in the region of the head of the pancreas, and there was a marked mesenteric lymphadenopathy. The small bowel was situated predominantly in the lower abdomen and to the left of the midline. Other than abnormalities resulting from displacement, the large and small intestines were negative. The head of the pancreas was displaced medially and anteriorily. The kidneys were normal in position and size on palpation, as was the spleen. Extensive dissection about the mass was not carried out nor were the extrahepatic biliary passages probed, inasmuch

as many previous authors have advised limited exploration once the operative diagnosis has been made in order to prevent unnecessary shock.

The posterior peritoneum overlying the cyst was incised, revealing the cyst wall to be quite thick. Using a tuberculin syringe and a hypodermic needle, several cubic centimeters of thin yellow bile were aspirated from the cyst. The abdomen was then carefully packed off with moist laparotomy pads and a trocar attached to a suction apparatus was introduced into the cyst. Seven hundred cubic centimeters of golden yellow bile were removed. A culture from this material was taken. Interestingly enough, as the bile was aspirated from the cyst, the gallbladder, which had previously been extremely tense, collapsed markedly. In view of the recommendations of other authors, notably Ladd and Gross, it was felt advisable to attempt immediate anastomosis between the cyst and duodenum without excision, either partial or total, of the former. The duodenum, because of its displacement, lay in an ideal position for a side-to-side anastomosis with the cyst. A biopsy of the cyst wall was obtained at this point, the wall being approximately 3 mm. in thickness, following which an anastomosis was effected. The stoma was situated in the first portion of the duodenum about one inch distal to the pylorus.

Following a complete change of gowns, gloves and drapes, a small biopsy was taken from the liver edge, the defect being closed with fine silk sutures. The wound was then closed in layers, using interrupted silk throughout.

During the operation the patient was given 500 cc. of whole citrated blood. He withstood the operation extremely well and returned to the ward in good condition.

Postoperative Course.—Almost immediately after operation the patient began to pursue a very stormy and hectic course. Unexplainable cyanosis was particularly troublesome during the first three or four days, making the administration of nasal oxygen imperative. Shortly after reacting from the anesthetic, the child began to vomit copious amounts of bile, necessitating the intermittent use of Wangensteen suction for seven or eight days. A marked tachycardia prevailed during most of the first postoperative week, and the temperature reached a peak of 102.6 on the fourth and fifth days; thereafter it began to subside. The skin sutures were removed from the wound on the sixth postoperative day, when the wound showed little evidence of normal healing. Abdominal pain was unusually severe and followed each attempt to take nourishment for many days. Parenteral supplementation consisting of Hartman's solution, 5% glucose, plasma, amigen, and blood were employed. Massive vitamin therapy, particularly large amounts of vitamin C and the B complex, and penicillin intramuscularly were also administered. Blood chloride on the third postoperative day was reported 525 mg.%. On the same day a red count was reported as 5.05 million with a hemoglobin of 112%, revealing some hemoconcentration. Moderate abdominal distention prevailed despite the use of the suction apparatus. On the eighth postoperative day, following a paroxysm of sudden vomiting, the wound disrupted throughout its entire length with eventration of small intestine. Sterile towels were immediately applied by the resident who was on the floor, and then the patient was taken to the operating room. His general condition was fair despite separation of the wound with protrusion of small intestine. A cannula was placed in the long saphenous vein, and he was given 250 cc. of plasma and the same amount of whole blood. It was noticed at the time of wound closure that the silk sutures were still intact, but there was no evidence of healing having occurred despite the postoperative administration of what had been thought to be adequate protein and large amounts of vitamin C. Following wound dehiscence with resultant evisceration, his course continued to be stormy, there being almost a persistent temperature to 100°. He gradually became able to take food, although for some weeks the ingestion of food caused some abdominal distention associated with cramplike abdominal pain. Normal-colored bowel movements were noticed on the tenth postoperative day. The silver wire sutures inserted at the time of secondary closure were removed on the twelfth postoperative day, when the wound had healed cleanly. Recovery of strength and weight was slow but progressive, and the

FIG. 2.—A photomicrograph of the cyst wall revealing the rather dense connective tissue and the lack of a definite lining membrane. (High power)

patient was discharged from the hospital on the twenty-seventh postoperative day asymptomatic and afebrile.

Pathologic Examination.—Microscopically the biopsy of the cyst wall was reported as showing moderately dense connective tissue which was relatively acellular and devoid of a proper lining (see Figure 2).

The biopsy of the liver histologically showed some excessive cellularity about the portal spaces and increased periportal fibrosis (see Figure 3).

The culture of the bile taken from the cyst revealed an almost pure growth of Escherichia coli.

Follow-up.—The patient was followed in the Outpatient Department for the first few weeks after discharge, his course for the most part being a steady improvement. Approximately six weeks after discharge from the hospital he experienced an episode suggestive of low-grade cholangitis, his mother stating that nausea, vomiting, temperature elevation, and a slightly icteric tinge to the sclera were noted. This attack, however, did not require hospitalization, his parents not even consulting the family physician, inasmuch as they had been warned before the child's discharge that such episodes might occur. He was last seen four months after operation, at which time he had gained approximately 5½ pounds and had been totally asymptomatic for two months.

COMMENT

The case presented would appear to be quite typical in practically all respects. The classical triad of mass, jaundice, and pain was present in this case, as were the less often emphasized symptoms of intermittent fever, occasional nausea and vomiting, and fluctuation in size of the mass. As would be expected, the findings characteristic of obstructive jaundice were present at the time the patient was admitted. Interestingly enough, as has been noted in the literature,[3] the condition had previously been diagnosed as acute catarrhal jaundice and, on a second admission, as acute hepatitis. McLaughlin[7] has remarked that an absolute preoperative diagnosis of choledochus cyst is impossible. However,

FIG. 3.—Photomicrograph of section of liver showing the increased cellularity about the portal spaces, as well as some increase in fibrosis. (Low power)

this case was considered to be such because of the typical and almost pathognomonic features of the case.

The surgical procedure carried out was that which apparently has been most generally recognized as giving the lowest mortality, namely, anastomosis of the cyst to the duodenum, which seems to us more accurately called choledochocystoduodenostomy than choledochoduodenstomy as in the past. Extensive dissection was not carried out, although more information could probably have been obtained by so doing. Inasmuch as most case reports, particularly those of Ladd and Gross,[6] have demonstrated that prolonged dissection has often resulted in high mortality, only enough exploration was done to confirm the preoperative impression. Although the immediate postoperative course was quite stormy and complicated by wound dehiscence with resultant evisceration, the patient at his last examination four months later was asymptomatic and had regained his preoperative weight of 43 pounds, his discharge weight being 37½ pounds. An episode resembling mild cholangitis occurred six weeks after operation, presumably from retrograde infection from the large cystic pouch.

Pathologic examination of the liver revealed some increased periportal cellularity and fibrosis, which in general conforms to the microscopic picture of the case reports in which liver biopsy was done,[14] although it was much less severe than in many. However, symptoms suggestive of marked liver involvement had subsided prior to the time of surgery. Examination of the cyst wall revealed a characteristic marked fibrosis with no evidence of a definitive lining membrane, this corresponding with most previous reports.[6, 11, 14] According to the literature, many different organisms have been cultured from the contents of the cyst.[11, 13, 14] B. coli, has often been found as was the case in this particular patient.

SUMMARY

A case of that unusual condition known as choledochus cyst diagnosed preoperatively and apparently successfully treated by choledochocystoduodenostomy has been presented, as well as brief comments on its rarity and historical aspects. It is discussed briefly in the light of previously reported cases. Four months after operation the patient is asymptomatic, although initially he pursued a stormy course.

"The most recent check-up was made in June, 1948, at which time the patient was totally asymptomatic and weighed 48 pounds, this representing a weight gain of 10½ pounds over his discharge weight."

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INTERNAL HERNIA WITH STRANGULATION OF BOWEL DUE TO A DEFECT IN THE FALCIFORM LIGAMENT *

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ALTHOUGH THE REGION of the umbilicus is the site of a wide variety of congenital lesions, the occurrence of abnormalities in the underlying structures, i.e., the round and falciform ligaments of the liver, is indeed a rarity. Trimingham and McDonald[1] have classified twelve different anomalies in the region of the umbilicus. They state: "The umbilical vessels converging at the umbilicus, persist, normally, as the two obliterated hypogastric arteries, and the ligamentum teres of the liver's falciform ligament. It is doubtful whether this process is ever subject to pathologic aberration." The author would like to present two cases of congenital defects in the liver's falciform ligament. In the first case, the defect in the falciform ligament was large and contained omentum. In the second case, the defect in the falciform ligament was small and contained a loop of ileum producing intestinal obstruction with strangulation.

The literature on intra-abdominal hernias is composed mainly of individual case reports, studies of limited groups of cases and reviews of special types of hernias. Moynihan[2], in 1906, published an excellent review of the various peritoneal fossae and reviewed the cases of intra-abdominal hernias up to that time. Short[3] reviewed the cases reported between 1906 and 1915, and in 1925, Short[4] reviewed the literature. Hansmann and Morton,[5] in 1939, published the latest review on the subject.

The author believes that the following case reports are of unusual interest.

CASE REPORTS

Case 1: I was called to see a 63-year-old white male who had severe pain in the umbilical region. He had been vomiting for several hours. His bowel movements were normal. The patient had been seen a few hours before by another physician who had made a diagnosis of gastroenteritis. Three years before, in another city, the patient had been jaundiced for two months. This was unaccompanied by abdominal pain or vomiting. Gall bladder roentgenograms had been taken, but the patient did not know the results.

Physical examination revealed no abnormalities of the chest. The abdomen moved with respiration and was soft on the left side. The whole right side of the abdomen was somewhat spastic with marked tenderness and rebound tenderness, more marked in the right upper quadrant than in the right lower quadrant. Rectal examination was negative.

The patient was hospitalized and had a temperature of 99.2°, pulse 120. Blood Count: Hemoglobin 109%. RBC. 6,050,000, WBC 17,000, neutrophiles 88, lymphocytes 8, monocytes 4, shift to the left. Urine showed a trace of albumin and was faintly positive for bile. Upright roentgenogram of the abdomen showed no air under the diaphragm.

The patient was taken to surgery with a diagnosis of acute surgical abdomen (perforated peptic ulcer or acute cholecystitis). On entering the peritoneum, the omentum appeared to blanket all the viscera and seemed to be running in several directions. Up through the center of the omentum extended what looked like a "guy rope" to the

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anterior abdominal wall. The disposition of the omentum appeared quite confusing, and only after dissecting it off the duodenum and gall bladder did the true situation become apparent. The fundus of the gall bladder was gangrenous and perforated, and had produced an intraperitoneal abscess which was walled off completely by the omentum. The omentum came up, as it usually does, to envelop the duodenum and gall bladder, but in addition, it had swung up around and through a large V shaped defect in the falciform ligament to again reach the duodenum and gall bladder. This "guy rope" piece of tissue was seen to be the obliterated umbilical vein, running from the porta hepatis to the umbilicus in the anterior abdominal wall, and the falciform ligament ended as a free edge, leaving a V shaped defect between the round and falciform ligaments. (see

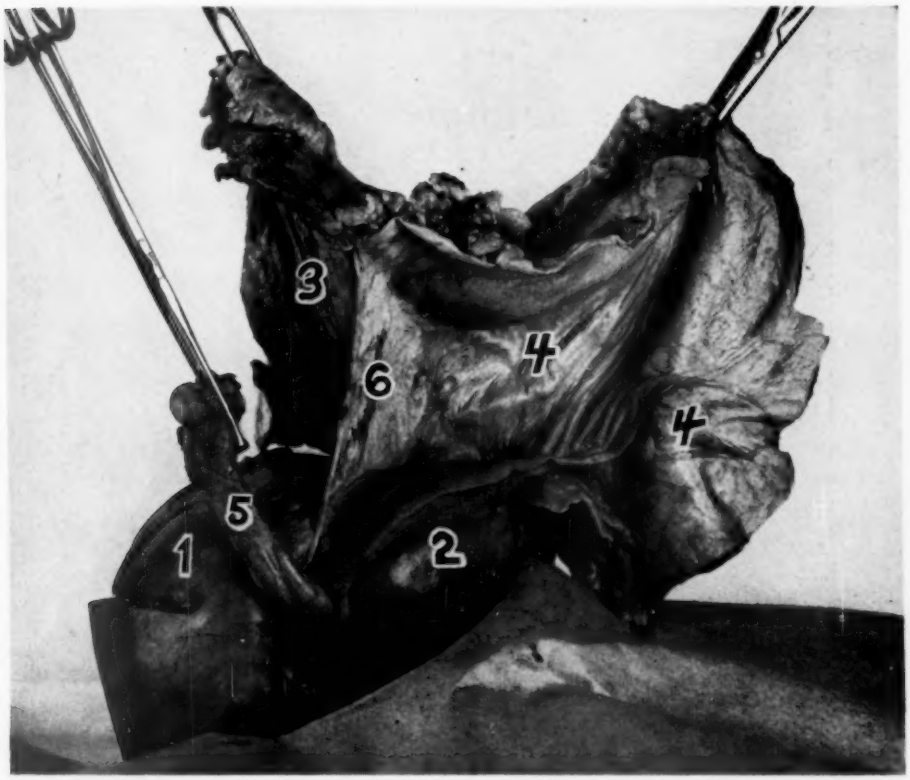

FIG. 1.—Anterior view of defect in falciform ligament with round ligament held up towards the anterior abdominal wall. (1) Right lobe of liver. (2) Left lobe of liver. (3) Parietal peritoneum covering undersurface of right leaf of diaphragm. (4) Parietal peritoneum covering undersurface of left leaf of diaphragm. (5) Round ligament. (6) Falciform ligament.

Fig. 1). No perforation was found in the gastro-intestinal tract. A cholecystostomy was done. The postoperative course was stormy and the patient died on the fourth postoperative day.

Autopsy revealed the described defect in the falciform ligament, associated with a lack of development of the left lobe of the liver, acute exacerbation of chronic cholecystitis with cholelithiasis, localized peritonitis, right retroperitoneal cellulitis, and coronary sclerosis.

Case 2: With the permission of Dr. Marcus H. Rabwin, Attending Surgeon at the Cedars of Lebanon Hospital, Los Angeles, I am presenting the following case which

occurred on his service. This patient had a similar defect in the falciform ligament with strangulation of the bowel.

A white male, 71 years of age, was admitted in a moribund condition and died in the hospital within a few hours, without operation. The patient gave a history of cramping, upper abdominal pain and vomiting for four days.

Examination revealed distention of the whole abdomen. Flat film of the abdomen

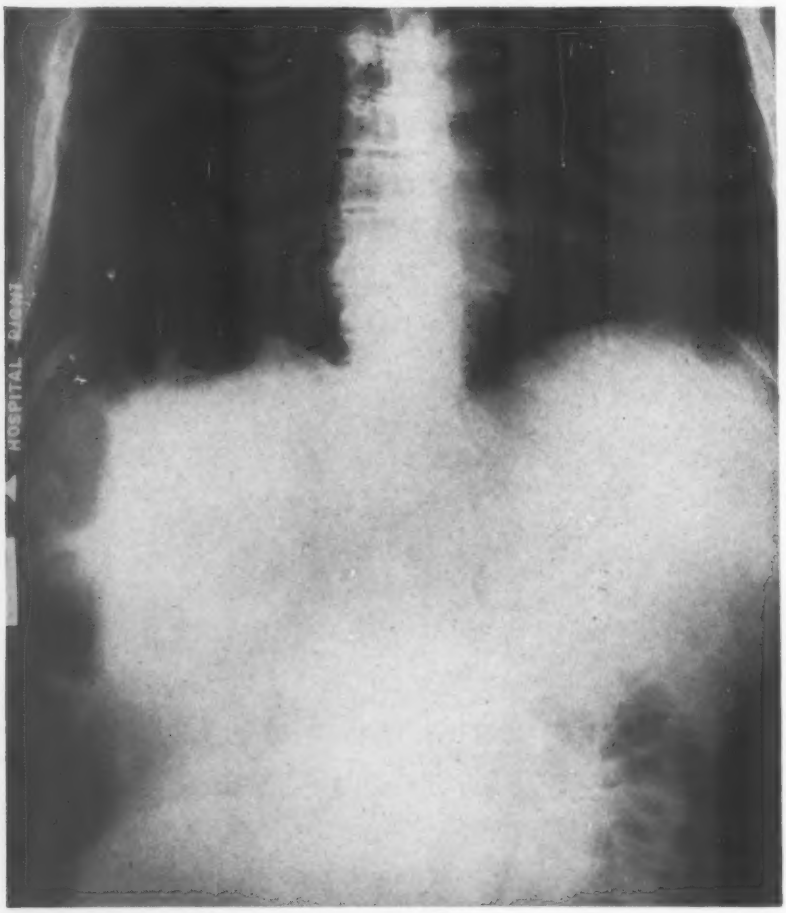

FIG. 2.—X-ray showing gas shadow in a closed loop of small intestine under right diaphragm. Also distended obstructed loops of small intestine down below.

revealed a gas shadow under the right diaphragm which was between the liver and diaphragm and was interpreted as free air.

At autopsy there was a loop of strangulated small intestine which had herniated itself through a defect in the falciform ligament. The cause of death was intestinal obstruction with strangulated bowel. After the autopsy, the flat film was reexamined and it became apparent that what looked like free air was actually a gas shadow in a closed loop of small intestine (see Fig. 2). Thus the diagnosis could have been made from this roentgenogram had we been aware of the existence of this rare condition.

DISCUSSION

A review of the literature discloses only one other report of an abnormality of this type. Schutz and Ziegler[6] report a case of intestinal obstruction due to internal hernia beneath the umbilical vein in a new born baby. The infant was operated on during the first week of life. At operation ten to twelve cm. of small intestine were found protruding through a small aperture just behind the ligamentum teres of the liver. The loop of intestine, as in our case, had entered the defect on the left side and had its exit on the right side, so that it again lay between the right lobe of the liver and the diaphragm.

Cullen[7] states that the peritoneum may be elevated over the umbilical vein in the form of a mesentery, but he makes no mention of an aperture between the vein and the anterior abdominal wall.

In one of the three cases, the defect in the falciform ligament was an incidental finding. Undoubtedly the occurrence of internal hernias is more frequent than one would think from the paucity of reports in the literature. This is so, because most of them exist without producing symptoms, just as patients frequently have asymptomatic external hernias. Alexander[8] has pointed out that internal hernias can be easily missed during a routine gastro-intestinal series. He advises observation of the small intestine at more frequent intervals by the radiologist. In the other two cases, the defect in the falciform ligament caused intestinal obstruction, and in one of these cases strangulation was also present.

Although internal hernias are uncommon they are important for the general surgeon because they may be met unexpectedly at the operating table. If the diagnosis could be made before operation, as shown in the photograph of the roentgenogram, it would be of vital importance.

Steinke[9] has classified internal hernias into three divisions: (1) Retroperitoneal (paraduodenal, paracecal, intersigmoid, supravesical and through the foramen of Winslow), (2) Intraperitoneal (anomalous openings in the mesentery, transverse mesocolon, omentum and broad ligament of the uterus), and (3) Postoperative after anterior or posterior gastroenterostomy and after the Baldy-Webster type of uterine suspension.

To the above classification, should be added a new group of internal hernias, i.e., hernias through defects in the falciform ligament. These defects undoubtedly are congenital anomalous openings and as such, should be included with internal hernias of the intraperitoneal type.

SUMMARY

1. Another group of internal hernias is added to the standard classification, i.e., hernias through defects in the falciform ligament.

2. The diagnosis may be made preoperatively.

3. An internal hernia is occasionally found as an incidental finding while operating for other conditions.

4. It is important to be familiar with internal hernias because it enables

the surgeon to recognize more quickly the condition at hand, and because reduction of the intestines can be effected with a cure.

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ACUTE TORSION OF THE GALLBLADDER *

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I. PURPOSE

The purpose of publishing this article on acute torsion of the gallbladder is to direct attention to an entity which is seldom mentioned in American medical literature, but which should be seen with increasing frequency in the future since it occurs predominantly in elderly people.

II. HISTORICAL DATA

In 1898 Wendel[14] reported the first case in a 23-year-old female. Shipley's article in 1927[12] revealed the 21 cases of torsion of the gall bladder reported up to that time and added one of his own. This was the most exhaustive study at that period. Short and Paul's (1934) classical discussion[13] is the most outstanding, both in comprehensiveness and clarity. The authors feel that the time spent in reading this excellent work is indeed worthwhile. Meeker and Lisenby's[11] recent work is especially desirable because of the beautiful plates depicting anomalies of the gallbladder.

III. INCIDENCE

As late as 1946 there were only 76 cases reported in the literature available.[5, 6] All reports indicated that the condition is found more frequently in females of the older age group, particularly of the visceroptotic type. According to Short and Paul,[13] 7 to 8% were males. The age of incidence varied from 11 years to 83 years. The vast majority, however, were between 60 and 80 years.

IV. MECHANISM OF TORSION

Four possible anatomic arrangements of the viscus are mentioned, only the fourth of which is important in our discussion:

1. Gallbladder may be embedded in the liver tissue.
2. Gallbladder may be closely attached to the under surface of the liver, with intervening connective tissue.
3. The outer surface of the fundus may be surrounded by peritoneum and the rest attached to the liver, but not actually touching because of the interposed fibrous tissue (the normal arrangement).
4. Gallbladder may be completely surrounded by peritoneum, and be free, except where it is attached to the cystic duct.

With the arrangement described in No. 4 above, it is conceivable that the

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cause of torsion is related to the movement of normal peristalsis in the transverse colon. As peristalsis proceeds, the overlying gall bladder becomes twisted. The associated abdominal rigidity aggravates the existing condition.

The matter of torsion, either clockwise or counter-clockwise, is still unsettled and is not important. The loss of elasticity of supporting structures is probably a factor, particularly in the old age group. The volvulus is more liable to reduce itself in a younger person because elasticity is still present. Stones do not seem to be a predisposing factor and are only present in a moderate percentage of the cases studied.

V. SIGNS AND SYMPTOMS

In the majority of cases the onset is acute, with sudden, severe pain in the right upper quadrant, or midabdominal pain which may radiate to the back or shoulder and in other characteristics simulate a biliary colic. Vomiting is a frequent, but not constant, finding.

In more than half of the cases reported it was stated that a palpable tumor mass could be felt in the region of the gallbladder shortly after the onset of pain (within two hours). This mass is usually exquisitely tender, can be seen or felt more readily with respiration, and is associated with rigidity and spasm of the abdominal muscles. Muscle spasm and rigidity of the abdominal wall increase with the duration of the symptoms. Jaundice is rarely present; in fact it was not mentioned in any case reported.

When the volvulus is incomplete the onset may be insidious, with less pronounced symptoms. Such cases are extremely difficult diagnostic problems because of their similarity to acute cholecystitis. Cases have been reported where the individual had severe pain and a palpable mass, both of which disappeared only to recur at a later time. Such a history should suggest the diagnosis of torsion.

Chills and fever are characteristically lacking. In fact, during the first 24 to 48 hours the temperature, pulse, and respiration are usually normal, but later all three may show a marked rise if surgical intervention is delayed.

Symptoms of peritonitis appear when the gallbladder becomes gangrenous and perforates. In only two reported cases has shock played a predominant role, and in one of these it was the apparent cause of death.

Flatulent indigestion, suggesting gallbladder disease, occurs infrequently in these individuals.

VI. DIFFERENTIAL DIAGNOSIS

Torsion of the gallbladder is most frequently diagnosed as cholecystitis or cholelithiasis, with hydrops or empyema of the gallbladder. Appendicitis, intestinal obstruction, twisted ovarian cyst, ruptured peptic ulcer have all been confused with this entity. However, in most instances, if the condition described herein is given consideration, diagnosis may not be too difficult.

Typically, torsion of the gallbladder occurs in an elderly visceroptotic female. The most striking symptoms are the sudden onset of severe epigastric pain (upper right quadrant), and the appearance of a palpable, tender mass a

short time later. The absence of jaundice, and constitutional symptoms such as fever, increased pulse and respiration, should suggest the diagnosis, especially if rigidity and tenderness are present on abdominal examination. Subsidence of the symptoms may occur if the volvulus becomes untwisted and the mass disappears. Likewise, the pain may be temporarily alleviated by manipulation of the tender mass, or by the assumption of various positions.

VII. PROGNOSIS

Hugh Arthur[2] mentions the mortality rate in cases of torsion as 16%. This could be reduced, however, providing an early diagnosis of the condition is made, since the chances for a successful operation and an early convalescence are excellent. All cases reported as having a fatal outcome either had perforated, expired from surgery, or were unrecognized on initial diagnosis.

VIII. TREATMENT

Early surgery will save the vast majority of cases recognized as torsion. The surgeon feels that a paramedian incision is the one of choice inasmuch as the tissue is loose and there is no difficulty in exposure. The cholecystectomy is simple but the general laxity of the tissues should make one extremely cautious, particularly in identifying the cystic and common bile ducts. One case of fatal outcome was caused by tying off the common bile duct. A few cases were reported to have had bloody drainage in the gallbladder fossa or peritoneal area. Early ambulation is essential.

IX. REPORT OF A CASE

The patient, R. P., a thin, 63-year-old white male, occupation—butcher, was first seen on 10/20/47. While at work three days previously, at 11:30 A. M., he was seized with a severe peri-umbilical pain associated with sweating and a feeling of faintness. The pain persisted without radiation; it was greatly aggravated by change of position and by coughing.

The evening of onset the patient vomited six or eight times, but this ceased the following morning and did not recur. The patient remained on a liquid diet throughout his illness, however. No belching, gas, distention, or bowel movements had occurred since two days prior to the onset of the present illness. There were no chills or fever, nor was there any jaundice. Pain, however, persisted.

In the past, the patient had had no similar episodes. However, at one time, about 30 years previously he had been treated for "ulcers"; these responded to a medical regime without recurrence. A review of systems, past health and family history did not reveal anything of note.

Physical examination. A tall, thin, 63-year-old white male, acutely ill, complaining of peri-umbilical pain; B.P. 120/76, pulse 78, resp. 18, temp. 99. The general physical examination was negative except for the abdomen, which on inspection presented a smooth, pear-sized mass, 1″ above the umbilicus, and to the right of the mid-line. This mass moved with respiration, and with the patient turned on his left side it could be seen and felt across the mid-line to the left epigastric region.

The mass was exquisitely tender to palpation and could not be well outlined because of the associated rigidity of the abdominal wall. At times it appeared to pulsate, but with the patient in knee-chest position no pulsation was evident. In this position, however, manipulation of the mass gave temporary relief of the pain, with recurrence of its former severity as soon as the recumbent position was resumed.

The patient was seen in consultation several hours later (90 hours after onset of

present illness), at which time the temperature was 100.2, pulse 106, respiration 24. The physical findings otherwise were essentially the same as on previous examination except for more extensive tenderness and rigidity. The impression was acute abdomen, probably a ruptured ulcer. The laboratory studies were as follows:

Roentgen-ray—flat plate of abdomen: normal except for a ptosis of right kidney
Urine—negative
White count—16,000; polys, 85; lymph, 15

Surgery. With the aid of a pontocaine anesthesia, the abdomen was opened, using a paramedian incision. A dark, shiny gallbladder presented itself and was attached only at the cystic duct; the neck of the gallbladder was twisted 360 degrees. The common bile duct was readily identified. No bloody drainage was present. The gallbladder was excised between two Moynihan clamps and the stump doubly ligated; the abdomen was closed without drainage. The patient was made ambulatory 12 hours later. Convalescence was smooth except for a cigarette cough. Sutures were removed on the eighth day. Patient returned for a 30-day checkup and was found fit.

Pathologic report. 1. Gross: Gall bladder measure, 8 x 4 cm. It is reddish black in color and appears entirely gangrenous.

2. Miscoscopic: Almost complete hemorrhagic infarction. One medium-sized artery contains an organizing thrombus and all the veins are enormously dilated and plugged with blood. One section shows extensive old chronic inflammation and fibrosis accompanied by marked glandular infiltration into the wall. This infiltration is in the form of strands and the epithilial changes are the result of chronic inflammation.

SUMMARY

A case of torsion of the gallbladder has been presented. A patient having a history of acute pain in the upper right quadrant, followed by an abdominal mass within two to three hours and a gallbladder syndrome, should make one consider this possibility, particularly in an elderly visceroptotic male or female. The authors hope the paper may be of some assistance in establishing such a diagnosis.

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SADDLE EMBOLUS OF THE AORTA

Report of Successful Embolectomy* †

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THE PURPOSE OF THIS PAPER IS to report an additional successful embolectomy at the bifurcation of the aorta. Although the literature of recent years[1, 2, 3, 4] records an increasing number of successful embolectomies for saddle embolus at this point, the total remains small. It is believed that the details of single case histories may still be of sufficient interest to justify a report of this kind.

CASE REPORT

Mrs. C. C., a 52-year-old housewife who had been confined to bed for several weeks, was recovering from her second episode of cardiac decompensation, during which she had received digitalis. Auricular fibrillation was present. Late in February, 1946, the patient noticed vague pain in the anterolateral part of the left leg. This was followed by weakness in the peroneal group of muscles and by a mild foot drop. About ten days later, on March 4, 1946, while the patient was out of bed to the bathroom, there was rapid onset of numbness in both legs, followed by pain in the lower abdomen and sacral region which moved downward gradually to involve both legs. At this time, the patient became unable to walk and paralysis of the lower legs was soon complete. A physician administered morphine, ¼ gr., without significant relief, while arranging for the patient's admission to Little Company of Mary Hospital.

The essential findings on admission were pain, coldness, numbness and paralysis of the legs, and diffuse pain in the lower abdomen and sacral region. The oral temperature was 96° F. Auricular fibrillation was present. The cardiac rate determined at the apex was 180 per minute. The pulse rate at the wrist was 80 per minute. The blood pressure in the left arm was 170/110 mm. Hg. Pulsation of the abdominal aorta could be felt distinctly almost to the region of the sacral promontory, but there were no pulsations below this point except for a weak pulsation in the region of the left femoral artery. This latter finding was interpreted as representing pulsation transmitted by a tail thrombus. A diagnosis of saddle embolus at the bifurcation of the aorta was made. Immediate embolectomy was advised.

Six hours after embolism, operation was performed. Under satisfactory general anesthesia, the bifurcation of the aorta was exposed transperitoneally through a midline incision which extended about equidistant above and below the umbilicus. (Fig. 3.) Pulsation in the aorta was present to within 2.5 cm. of the bifurcation. Below this point, a soft mass extending into both iliac arteries could be palpated through the walls of the vessels. The overlying peritoneum was divided, and the aorta and the iliac arteries in the region of the bifurcation were freed from the surrounding areolar tissue. Tapes were placed about the aorta and the iliac vessels, and an incision about 2 cm. long was made into the anterolateral portion of the vascular wall at the junction of the aorta and the right common iliac artery. (Fig. 1.) The obstructing mass of clot was removed from the region of the bifurcation, together with a tail thrombus about 6 inches long from the the right iliac artery. (Fig. 2.) The clot was removed from the left iliac artery in several pieces and free bleeding occurred with the force expected as each tape was released inde-

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pendently. The opening in the vessel was closed by a running mattress suture of fine "arterial" silk which everted the edges, producing intima-to-intima contact (Fig. 1), and at this time the intravenous administration of 10 cc. (100 mg.) heparin solution in 500 cc. normal saline solution was begun. The abdomen was closed. The patient's general condition was considered fair, the blood pressure having fallen from 140/80 to 110/60 during the operation, while the pulse rate varied from 100 to 140 per minute. The operation lasted 115 minutes.

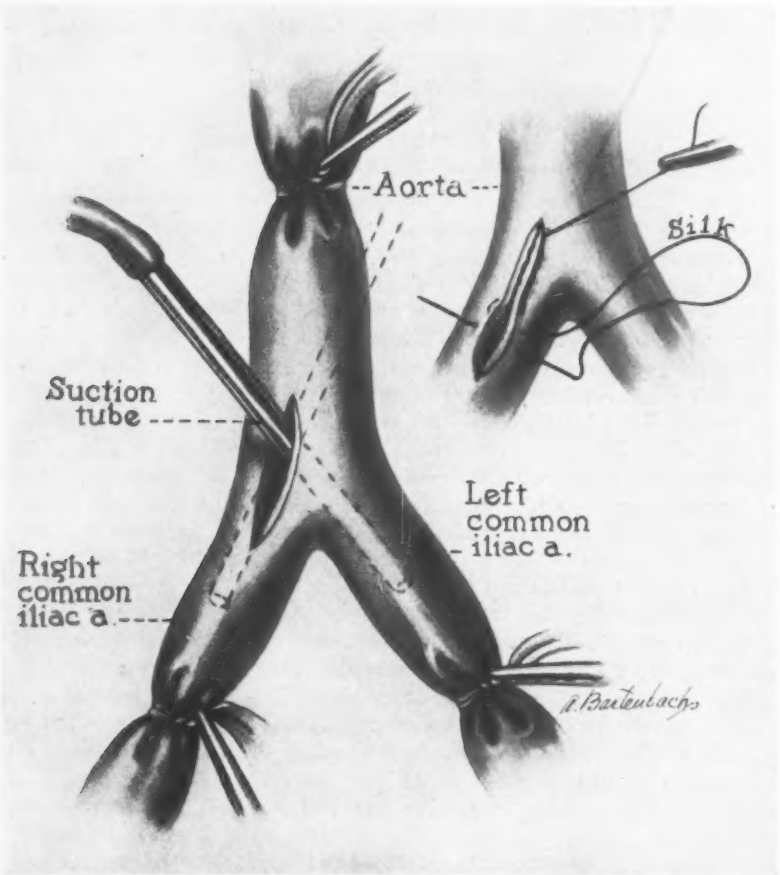

FIG. 1.—The incision in the vessel wall at the junction of the aorta and the right iliac artery is shown. By opening the vessel at this point, the mass of clot accumulated at the bifurcation was easily removed and it was possible to pass a suction tube into both iliac arteries. The tapes maintained hemostasis satisfactorily and apparently did not damage the vessel walls. In closing the incision, a single running mattress suture of 5-0 silk provided intima-to-intima approximation.

Immediately after the operation, pulsations could be felt in all peripheral arteries except the dorsalis pedis on the left. On the following day, paralysis of the peroneal group of muscles on the left was found to be present. The postoperative course was otherwise satisfactory. On the 5th day following operation, pulsation returned in the dorsalis pedis artery on the left, but marked weakness persisted in the peroneal group of muscles for about four weeks. Adjunct treatment consisted of novacaine injection of the lumbar sympathetic fibers bilaterally on the first postoperative day, spinal anesthesia (pontocaine

hydrochloride) on the second, third, fourth and sixth postoperative days, intermittent venous constriction, and anticoagulant therapy. The patient was allowed to be out of bed on the 12th postoperative day and was dismissed from the hospital 5 days later. Dependent edema of the left leg was present for about 6 weeks following the operation (Fig. 3), but was easily controlled by elastic bandages and has not recurred. During the summer of 1946, the patient enjoyed a 4,000-mile motor trip with her family. She has resumed and continued light household duties. Mild weakness of the peroneal muscles on the left persists. In the 23 months which have elapsed since operation, the heart disease has remained compensated. Fibrillation, however, is still present.

DISCUSSION

Embolic occlusion of any of the major arteries is not only a serious condition *per se;* it also indicates the presence of major underlying disease. The source of the emboli is most often the heart. Rheumatic endocarditis, particularly with mitral stenosis, and upon which have been superimposed the factors of infection, operative trauma, fibrillation, or coronary occlusion, is the most frequently encountered basic pathology. Murray[5] states that in coronary disease the mural thrombus may attain such size that portions of it are not firmly attached and can be swept into the circulation. Far less commonly, vegetations from heart valves, atheromatous plaques from the aorta, or the unusual paradoxical embolus arising in the course of venous thrombosis[6, 7, 8], cause embolic obstruction in the major arteries. Changes in the clotting mechanism associated with intensive or excessive digitalis dosage, as described by De Takats et al,[9] must be included in the etiologic background. Murray[5] and Reynolds and Jirka[10] have called attention to the influence of changes in cardiac rate and rhythm in dislodging emboli. Thus, the onset of fibrillation or the restoration of normal rate and rhythm are often associated with embolism.

FIG. 2.—The clot as assembled after removal. The tail thrombus is from the right iliac artery and was approximately 15 cm. long. The clot from the left iliac artery was removed in several pieces.

Obstruction at the bifurcation of the aorta due to a saddle embolus is the most serious of all peripheral embolic disturbances and, fortunately, the least common, comprising approximately 4.5 per cent, according to Pratt.[11] However, De Takats' compilation[12] of the figures given by Heidrich,[13] Petitpierre[14] and Pearse[15] places the incidence of saddle embolus at 10.14 per cent.

The patient with obstruction of the artery to an extremity, if untreated, may develop gangrene and survive subsequent amputation. It is generally conceded, however, that in every instance of aortic embolus obstructing the

bifurcation in which the circulation is not restored, the patient is doomed to death from gangrene.[5, 12] The extremely rare reports in the literature[16, 17] which describe spontaneous recoveries of patients with saddle emboli of the aorta may concern partial occlusion with subsequent thrombosis occurring in such a manner as to permit the collateral circulation to become adequate. Another explanation may be the occurrence of simultaneous or almost simultaneous bilateral iliac or femoral emboli. Thus, in Reich's[16] case of aortic obstruction with recovery under conservative management, the patient had pain in hips and legs but no abdominal pain. It is not stated that both femoral pulsations were absent. The patient showed considerable improvement on the second day. Herrman's[17] case, diagnosed as saddle embolus of the aorta, had pain first behind one knee and, several hours later, behind the other knee. He had "fleeting pain in the abdomen and precordium." The femoral pulsation, barely palpable on the left, was not definitely palpable on the right.

FIG. 3.—This photograph was taken a short time after dismissal from the hospital. The wound is healed solidly. The swelling of the lower part of the left leg can be seen. There was no significant difference in color or skin temperature of the right and left legs.

DIAGNOSIS

The onset of persistent peripheral circulatory disturbances of severe degree in a patient whose medical background contains any of the above-mentioned etiologic factors should, until proved otherwise, warrant a diagnosis of peripheral arterial occlusion. The visual conception of the speed of arterial blood flow and the sudden arrival of an embolus at a point in the vascular system so narrow as to be completely blocked by the embolus make it easy to believe that the onset of symptoms (in peripheral arterial embolus) must be sudden. However, two general types of histories have been obtained in proven cases. One of these is characterized by sudden localized pain indicating approximately the point at which the embolus has been arrested and, after an interval lasting up to several hours, a diffuse type of aching pain throughout the areas distal to the obstruction, due principally to anoxia of the muscle and varying in degree with the amount of muscle involved. This clinical picture is ascribed to obstruction of the main artery, accompanied by vasospasm to a small degree proximal to the embolus, but principally distal, with subsequent thrombus formation blocking the collateral circulation. This sort of clinical picture is present in approximately two-thirds of the reported cases of peripheral arterial embolus.[3, 5, 18] It appears to be even more frequent in saddle embolus of the aorta, according to the review of

McClure and Harkins,[2] who found it present in 97 per cent of the cases reported by Hesse.[19] The other mode of onset seen in the remaining third of reported cases of peripheral arterial embolus is characterized by paresthesia as the initial symptom, followed by numbness, diffuse pain and paralysis as anoxia becomes more severe. The case reported herein and those reported by Ravdin[20] and Linton[3] had this type of history.

Murray,[5] in commenting on the difference in the symptomatology, pointed out that the smaller arteries near the periphery have a greater proportion of smooth muscle in their walls than do the larger central vessels and, therefore, may be the site of more severe vasospasm and pain. He states that in his cases of aortic and iliac emboli the pain at the onset was not as severe as in some of the more peripherally located emboli. Agar's patient,[4] treated successfully by embolectomy for saddle embolus at the aortic bifurcation, complained only of numbness followed by "discomfort." With relatively less smooth muscle in the larger vessels, there should be less vasospasm and hence less pain. For the same reason, one would expect less pain at the onset in patients whose vessels have atheromatous changes. The complete absence of pain as reported by de Takats[21] could be explained on the basis of one of these factors plus ischemia, which brought about an early physiologic block of sensory nerves.

According to Murray,[5] the absence of pulsations is the most important sign; yet, this finding is subject to careful consideration and analysis. Vasospasm may be so severe as to obliterate pulsations in vessels not obstructed by clot, as reported by Atlas[22] and by Reynolds and Jirka.[10] In these instances, the pulses may return while preparations for operation are being made. It must be concluded in these cases that an embolus has moved distally or that vasospasm has subsided. On the other hand, the presence of pulsations may be deceiving. Theoretically, the transmission of pulsations by a tail thrombus should produce a linear thrust (Nordentoft's sign) instead of an expansile type of pulsation, but this distinction may be difficult in the presence of much subcutaneous tissue. If the patient is not too obese, pulsations can be felt in the aorta above the embolus. The clearly defined point beyond which they are not palpable is often striking.

Tenderness at the site of embolus is not present early, but depends on the development of inflammatory changes in the intima. The color changes in the skin are important. Pallor and blanching occur early; later, mottled cyanosis appears. Leriche[23] has called attention recently to "marbled" blanching which, he warns, means complete arterial obstruction. He states that antispasmodic drugs and blocking of the sympathetic fibers are insufficient to restore the circulation at this stage and that surgical intervention is imperative. Later manifestations include motor and sensory paralysis, as ichemia produces a physiologic interruption of nerve and muscle function.

With the etiologic factors and symptomatology in mind, it would seem almost impossible to confuse the clinical picture of aortic embolus with the more gradual process of aortic thrombosis. In the latter, there are usually

weeks or months of development characterized by fatigability of the lower extremities, intermittent claudication, coldness of the feet, atrophy of the calves and thighs and, in males, impotence.[24] Most of Greenfield's patients[25] were seriously ill with some systemic disease or already had complications of their heart disease. However, in cases of thrombosis the circulation may become inadequate rather suddenly (in 10 per cent of cases, according to McKechnie and Allen[18]), and the onset of pain and evidences of circulatory inadequacy may therefore appear to be an acute and recent process. The differentiation should be made easily on the basis of the past history, the atrophy of the legs, and sclerosis of peripheral and retinal vessels. In many instances, roentgen-ray examination will show calcium deposits in the peripheral vessels.

Phlebothrombosis, characterized by pain and coldness and accompanied by sufficient vasospasm to obliterate palpable pulsations, might be confused with arterial occlusion, but it is unlikely that both extremities would be involved simultaneously. Furthermore, the events leading up to it, the lack of etiologic background for an embolus, its unilaterality, and the continued presence of sensation and voluntary motion should enable one to make the distinction.

TREATMENT

Embolectomy is the only life-saving treatment for a patient with an aortic embolus. Even in poor risk patients it is well to remember that they do not die from the operation of embolectomy: they die of gangrene, heart disease, or as a result of amputation. As a general rule, the sooner embolectomy is done, the better will be the results. Furthermore, as Pratt states,[11] thrombosis follows embolus in 50 per cent of cases and will spread to involve collateral vessels. This is one of the main reasons for early operation.

Morphine given for the pain will generally serve as the pre-anesthetic medication, with the addition of scopolamine or atropine. Two approaches have been used: one a direct attack by exposing the bifurcation of the aorta[1, 3] and the other, an indirect approach in which the iliac or femoral arteries are exposed and the clot dislodged by the retroperitoneal milking of Nyström[26] or by intravascular probing.[10, 20, 27] In the indirect methods, the clots are swept down by the pressure of blood behind them and removed from the vessels at or near the inguinal ligaments.

The general condition of the patient will be the deciding factor in the choice of operative procedure. There will be patients who are obviously extremely poor risks for the transabdominal approach and whose only hope lies in the success of the indirect removal of the clot. If the general condition of the patient warrants the abdominal approach, it appears to be a matter of choice whether one opens the peritoneum or not. Murray[1] finds the retroperitoneal approach entirely satisfactory. The time necessary to do the retroperitoneal dissection is probably about the same as that needed to close the peritoneum when the transperitoneal approach is used. Since the bowel is packed out of the way and need not be disturbed throughout the operation by the transperitoneal route, there should be little trauma to cause postoperative ileus; whereas it is well known that troublesome ileus may result from retroperitoneal dissection. A

special indication for the retroperitoneal approach might be the presence of intraperitoneal infection or suppuration. In such a case reported by Schmorell,[28] in which a saddle embolus of the aorta occurred in the presence of peritonitis following operation for appendicitis, the extraperitoneal milking method of Nyström was employed successfully.

Anesthesia will depend on the approach. The indirect approach through the femoral vessels can be made largely under local anesthesia. For the transabdominal route or for the deeper portion of the retroperitoneal milking skillfully given general anesthesia supplying adequate oxygen with the anesthetic agent is preferred. Two objections to spinal anesthesia have been expressed. One is that the relaxation it brings about in the vessels may allow the embolus to migrate, and it does not necessarily follow that it will go to a more accessible point. The other objection is that often there may be a fall in blood pressure with the spinal anesthetic contributing to the stagnation of blood and enhancing the chances of thrombus formation. However, Agar's successful case[4] was performed under spinal anesthesia.

The next point to consider is the method by which the lumina of the aorta and the iliac vessels are temporarily occluded. If the walls of the aorta and the iliac arteries are normal or, at least, not atheromatous, occlusion by the use of umbilical tape, clamping it close to the vessels and twisting the clamp, as apparently has been done in most of the reported cases, appears to be entirely satisfactory. The use of modified Moynihan intestinal clamps, as used by Gross in aortic resection for coarctation,[29] and the Bethune clamp, as recommended by Linton,[3] would cause less wrinkling of the intima and, perhaps for that reason, less chance of disrupting it.

There are few references in the literature describing the incision in the aorta.[3, 5] The anterolateral incision at the junction of the aorta and the right common iliac artery, as shown in Figure 1, is entirely satisfactory. In addition to providing adequate room for removal of the mass of clot at the bifurcation, it permits the introduction of a suction tube into both iliac arteries for the removal of any clot which has not adhered to the main mass. The incision in the vessel wall is about 2 cm. to 2.5 cm. long. It is believed that a smaller incision would necessitate breaking up the mass of clot, thus running the risk of a small piece being overlooked and swept distally on re-establishment of the circulation.

Usually it is not difficult to remove the clot resting at the bifurcation of the aorta. If this is done before clotting has occurred in the collaterals, a single tail clot (Figure 2) will come with it. However, if the clot becomes fragmented, suction by means of a glass tube or a catheter with the opening on the end may be used to retrieve clot fragments. It seems reasonable to suppose that clots in the smaller vessels and portions of the main clot which are still present in the larger vessels might be "milked" proximally to the site of embolectomy by wrapping the leg firmly from the toes upward with a wide Para rubber bandage. Often, the small remaining portions of clot so impair the circulation as to prevent survival of the extremity after what appears to be a satisfactory embolectomy. This wrapping could be used, for the same reasons, in embolec-

tomy in the upper extremity and, because of the lesser muscle mass, might be more effective there.

The closure of the wound in the aorta is not difficult. The running mattress suture used here (Fig. 1) was entirely satisfactory. This is the same stitch as that used by Gross[29] in re-establishing the continuity of the aorta after excising the area of coarctation. One might believe that the success of such a closure would depend on the condition of the aortic wall and, in the presence of atheromatous changes, be inclined to reinforce the suture line with fibrin foam, oxycel etc., supported by an encircling cuff of chromic catgut as described by Jenkins.[30] Fascia as a reinforcing material might be considered, since an adequate supply would be available from either the anterior or posterior rectus sheath. However, in the cases reviewed by McClure and Harkins,[2] there was no instance of secondary hemorrhage as the cause of death.

As in other blood vessel surgery, the increasing number of successes is, to a large degree, due to the use of anticoagulants. Since the vessels of the lower extremities are the most likely places for the occurrence of postoperative thrombosis, heparin may be injected directly through the suture line in the aorta and be carried immediately into the vessels of the legs. It can also be given in the form of continuous intravenous drip, but the cardiac status of these patients warrants caution in determining the amount of fluid to be given this way and in its rate of administration. More recently, heparin has become available in a vehicle designed to permit slow absorption which, if effective, may simplify matters. As soon as the stomach is retentive, the administration of dicoumarol may be started. When the prothrombin activity has been sufficiently depressed, heparin may be discontinued.

Other postoperative measures of importance are attempts to dilate the vessels of the extremities either by interruption of the sympathetic fibers or by mechanical means, such as the use of intermittent venous occlusion or the alternating positive and negative pressure (Paevex). In the case reported herein, it seemed much more simple to administer a spinal anesthetic in order to provide vasodilatation bilaterally than to subject the patient to bilateral sympathetic blocks. One of the longer-acting agents (pontocaine) was used without untoward incident.

CONCLUSION

A case of successful removal of a saddle embolus of the aorta is reported. From a review of the available literature, it appears to be the 22nd case of this kind. Some general points in the etiology, diagnosis and management are discussed.

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THE HISTOCHEMISTRY OF BURNED HUMAN SKIN*†‡

With a Note on Base Exchange in Traumatized Tissue

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THE REQUIREMENTS OF THE BURNED PATIENT for sodium in therapy has been a subject of investigation and controversy in recent years. One aspect of this problem has turned on the question of whether or not there is a "selective" or "excessive" need for sodium in therapy. By this has been meant a need for sodium over and above that required to satisfy extra-cellular requirements; a need larger than that which could be satisfied by sodium in isotonic concentrations.

There are two mechanisms which might conceivably operate to produce such an excessive need for sodium. One would be the presence of sodium in increased concentration in the edema fluid of the burn, the other its presence in high concentration in the intracellular water. There is no evidence that the former exists; what knowledge we have of the burned capillary would indicate that burn edema fluid is in ionic equilibrium with other extracellular fluids. If the viable capillary allows Na and Cl to remain at essentially the same concentration on its two sides, there is little reason to postulate that the damaged capillary of the burn would be able to do the osmotic work required to bring about a concentration gradient.

Analyses of whole burned limbs[1] or observations on human patients given radiosodium[2, 3] do not yield data on selective sodium loss into the burn, since the increased tissue water in the area of the burn[3] would yield increases in apparent sodium volume and turnover even though concentration were not increased; the need thereby imposed could be met by the administration of isotonic sodium solutions.

In contrast to this extracellular isotonicity, the situation in the cell may be quite different. With sodium present in only small quantities normally, its ingress in increased amount—possibly in exchange for normal intracellular cations such as potassium or magnesium—could, theoretically at least, place a severe demand on body sodium resources, a demand which would not be met by isotonic sodium because, in exchanging for K, the sodium could move into the cell without a net water transfer[4].

For this reason we have sought to investigate the histochemical changes in burned skin. Skin was chosen because of its obvious relation to the trauma,

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and its accessability for study. Because of the normally small intracellular phase of skin it is a tissue unlikely to show quantitatively large cation transfer in response to trauma.

Electrolyte metabolism, as viewed in the burned patient as a total organism, is described in other investigations from this laboratory.[3, 5] Amongst other salient points the observation was made that the exudate loss of sodium often exceeded many times that of other routes of excretion.[5] Because of this permeation of sodium ion (and to a lesser degree chloride) through the burned tissue, the chemical composition of the burned tissue itself acquires additional importance.

METHODS

1. *Clinical.* Ten patients were selected, with both deep and superficial burns. Skin was removed for study under varying conditions. In deep full thickness burns generous portions of skin may be removed without anesthesia since the burn has destroyed the sensory nerve-endings; in some instances pentothal anesthesia was used, in others local anesthesia, care being taken to avoid introducing water directly into the portion to be studied. In two extensively burned patients who died within ten days of their injury the skin was removed immediately post mortem.

Unburned skin was also removed from burned patients for study, employing areas contralaterally symmetrical to the burn, so as to obtain skin of like thickness and histologic composition for comparison with burned tissue.

Skin was removed from healthy, unburned persons for control observations.

If radiosodium (Na^{24}) studies were to be made, the Na^{24} was injected as isotonic saline (0.5 to 0.75 mc. in 10-30 cc.) from one to five hours prior to the biopsy.* It was considered important to take the skin samples soon after radiosodium injection so as to bring out any differences in sodium exchange. If such a diffusible ion as Na is allowed to achieve physical (isotopic) equilibrium for 12 hours or more, acute differences in rate of uptake will not be demonstrated. In 12 to 24 hours equilibrium specific activity ratios (Na^{24}/Na^{23}) will have been reached throughout most of the tissues, and minor permeability changes will not become apparent.[6]

2. *Na^{24} Analyses.* Immediately after removal from the patient the skin was mechanically freed of subcutaneous fat and weighed in portions 0.5-1.5 grams in size. Two, three or four such samples were prepared from each site, placed in a porcelain ashing capsule and ashed at a temperature safely below the volatilization point of sodium.†

* Radioactive sodium (Na^{24}) was prepared by the deuteron bombardment of metallic sodium at the Massachusetts Institute of Technology cyclotron. This sodium metal was then hydrated and neutralized, the resultant Na^{24} Cl being used for injection in patients after suitable sterilization by autoclaving.

† Control observations indicated the greater accuracy and reproducibility of this technic as compared with wet ashing methods, or nitric acid extract.

The radioactivity determinations were then carried out on this dry ash of skin, in the ashing capsule, by means of a Lauritsen quartz-fiber electroscope. Appropriate corrections for decay and self-absorption were made prior to calculation of the results.

3. *Water and Salt Analyses.* After radioactivity analysis the dry ash of skin was quantitatively transferred to glass and analyzed for Na^{23} by the method of Butler and Tuthill.[7] In a few cases chloride analyses were carried out, using the method of Wilson and Ball on a solution made of the dry ash.[8]

Duplicate tissue samples, after weighing, were taken to dryness at 90°C and then re-weighed to determine water content. These were then ashed and analyzed for sodium and chloride to corroborate the observations obtained from the samples used for Na^{24} determinations.

Much histochemical work, especially that based on analyses of muscle and viscera, is expressed on a fat-free basis. This is because of the fact that deposits of neutral fat add a variable weight increment which is relatively free of water-soluble constituents. The fat-free results therefore exhibit a lesser standard deviation from the mean and are more acceptable statistically. Skin, considered as dermis and epidermis only, contains relatively little neutral fat in fat cells; vigorous defatting procedures doubtless remove intracellular lipoid-soluble material and squamous epithelium whose presence is necessary to the adequate description of the tissue. For these reasons and the fact that defatting skin (as opposed to other tissues) does not readily bring the tissue to constant weight, we have avoided defatting procedures in these studies. This results in a lower electrolyte content per unit skin by weight than one finds in "fat-free" skin.

4. *Calculations.* Na^{24}, Na^{23}, chloride and water were calculated in relation to the weight of wet tissue (e.g. mE per Kg. wet tissue) and to the weight of tissue water (e.g. mE per Kg. tissue water). The calculations of extracellular space based on sodium and chloride concentrations were carried out by the formulas of Hastings and his group.[9] Other figures, derived from these fundamental calculations, will be described below.

Observations

1. Sodium content in terms of tissue weight

a. Normal Skin of Unburned Patients. In Table I is shown the sodium content of the normal skin of unburned patients. The mean sodium content in 21 such specimens was 74.0 mE per Kg. of wet tissue. Standard deviations* represent about 10 per cent of the mean. These values run consistently lower than those reported by other workers who subjected the skin to a fat-freeing process. The work of Manery and Hastings based on fat-containing tissue in the rabbit is in the same order of magnitude as our results.[12]

b. Unburned Skin of Burned Patients. In Table II is shown the sodium content of the unburned skin of burned patients which appears to average about 10 mE/Kg. of wet tissue higher than the normal skin of unburned patients. This may be traceable to parenteral saline administered though it is

* $\sigma = \sqrt{\frac{\Sigma d^2}{n}}$

TABLE I.—*Sodium Content of Normal Skin.*
mEq/Kg. Wet Tissue
NORMAL SKIN OF UNBURNED PATIENTS

	No. of Samples	Mean	Standard Deviation
Pt. Mo.	10	78.86	± 4.51
Pt. McC.	7	66.8	± 6.96
Pt. Mc.	1	65.2	
Pt. A.	3	78.0	± 7.15
Total	21		
		74.0 (Average of all Samples)	
Eisele & Eichelberger (10)	18	93.0	± 8.0 (Fat-free)
Eichelberger et al (dog) (11)	..	96.5	± 4.2 (" ")
Manery & Hastings (rabbit)(12)	..	79.6	

TABLE II.—*Sodium Content of Skin.*
mEq/Kg. Wet Tissue
UNBURNED SKIN OF BURNED PATIENTS

Case Number	No. of Samples	Mean	Standard Deviation
254	3	72.0	± 3.87
229	3	76.6	± 5.17
231	2	79.1	± .01
217	2	82.75	± 2.75
234	3	88.3	± 2.5
210	1	88.6	
240	3	89.6	± 7.95
225	6	96.0	± 5.56
Total	23		
		85.5 (Average of all Samples)	

Case Number	FULL THICKNESS BURNED SKIN No. of Samples	Mean	Standard Deviation	PARTIAL THICKNESS BURNED SKIN No. of Samples	Mean
217	1	80.3			
234	4	81.7	± 6.67		
240	5	86.0	± 3.16	3	86.0
254	4	92.5	± 2.28		
229	3	95.8	± 5.56	4	82.2
210	3	98.1	± 4.54		
231	3	99.6	± 4.03	3	82.0
225	4	117.2	± 2.95	2	103.0
Total	27			12	
		94.5 (Average of all Samples)			89.0

of interest that some of the higher sodium contents were observed in patients who, because of the limited extent of their burns, received very little (or no) parenteral therapy.

c. Burned Skin of Burned Patients. In Table II are also shown values obtained from the burned skin of these same patients; an elevation of sodium content amounting to about 10 mE/Kg. of wet tissue as compared to the unburned skin is observed.

The burned skin from superficial (partial thickness) burns shows distinctly less increment.

The sodium content of full thickness burned skin shows more variation than the other data, for reasons to be described below.

d. Sodium Ratios in Burned Skin. Although the arithmetic mean of sodium content in burned skin is higher than that of unburned skin in the same patients, a more significant calculation is the ratio of sodium content in burned skin to that of contralateral unburned skin in the same patient.

Such findings are summarized in Table III. It will be seen that of these ten patients with deep burns, six showed a significant increase in sodium con-

TABLE III.—*Sodium Ratios.*

Case Number	Mean Sodium Content	Burned Skin Full Thickness / Unburned Skin	Burned Skin Partial Thickness / Unburned Skin
234	0.93		
240	0.96		0.96
217	0.97		
196a	1.09		
210	1.11		
225	1.20		1.07
229	1.25		1.07
231	1.26		
254	1.28		
205	1.30		1.04
Mean of Series	1.14		
Values between 0.90 and 1.10—No Significant Change			
Mean of Ratios Showing Significant Change	1.23		

TABLE IV.—*Water Content of Skin.*

Gm./Kg. Wet Tissue

NORMALS

	Range	Mean	Standard Deviation
Eisele & Eichelberger (10)	677 - 756	717.7	± 20.1
Eichelberger et al (dog) (11)		708.3	± 20.1
Manery & Hastings (rabbit) (12)	670 - 694	682.0	± 12.0
Massachusetts General Hospital	578 - 678	630.0	± 32.6

BURNED PATIENTS

Case Number	Full Thickness Burn	Full Thickness Unburned	Full Thickness Burn / Unburned	Partial Thickness Burn / Unburned
(A) Under 3 days after burn				
240	675	680	0.99	1.01
254	660	630	1.05	
225	790	730	1.08	0.98
229	758	659	1.15	1.12
217	844	704	1.20	
196a	693	581	1.20	
Average of Ratios under 3 days			1.11	
(B) Over 3 days after burn				
210	707	754	0.80	
205	640	720	0.88	
234	661	739	0.89	
231	622	671	0.92	
Average of Ratios over 3 days			0.87	

tent. The whole series taken together showed a mean increase in sodium content of 14 per cent and those showing any increase at all showed an average increase of 23 per cent in the amount of sodium present. These same ratios for partial thickness burned skin are very close to unity, indicating no significant increase in the sodium content of superficially burned skin.

2. SODIUM CONTENT IN TERMS OF TISSUE WATER

If the burned tissue were simply edematous from collections of extracellular water, an increase in tissue water commensurate with the sodium increment should be observed; under such circumstances one would predict little or no alteration in sodium content expressed relative to tissue water rather than tissue weight.

Table IV and Table V contain data relative to this point. The water content of the skin observed in this series (Table IV) is somewhat lower than that found by Eisele and Eichelberger in normal skin which, as mentioned

TABLE V.—*Sodium Ratios in Tissue Water.*

Case Number	Mean Sodium Content Tissue H_2O mEq/Kg. Tissue H_2O	Burned Skin Full Thickness / Unburned Skin	Burned Skin Partial Thickness / Unburned Skin
196	0.78		
217	0.80		
240	0.98		0.95
225	1.00*		0.86
234	1.02		
229	1.13*		0.95
210	1.17*		
254	1.22*		
231	1.38*		1.02
205	1.46*		
Mean of Series	1.09		
(mEq/Kg. Wet Tissue)	1.14		
Mean of Increases	1.27		
(mEq/Kg. Wet Tissue)	1.23		

Values between 0.90 and 1.10 — No Significant Change

* Indicates patients showing significant increase in sodium content mEq/Kg. wet tissue

before, has been subjected to a fat-freeing process. It will be noted that in the fresh full thickness burns (less than three days duration) there is an increase in water content (as compared with the unburned tissue) amounting to 11 per cent. There are too few observations on partial thickness burns to be significant. In burns which occurred more than three days before the study was made, the ratios are consistently below 1.0 and show approximately a 13 per cent decrease in water content.

These figures indicate that freshly burned skin is in a state of water collection probably correlated with changes in capillary and cell permeability; this acute situation yields later to dehydration presumably due to loss from the sur-

TABLE VI.—*Radiosodium Uptake of Skin.*
Specific Activity = Units of Radioactivity

Case Number	Specific Activity Full Thickness Burn	mEq. of Sodium Specific Activity Unburned	Full Thickness Burn Unburned	Partial Thickness Burn Unburned
(A) Under 3 days after burn				
196a	3.03	3.62	0.84	
229	4.73	4.55	1.04	
217	4.87	4.49	1.08	1.06
240	9.52	8.25	1.14	1.03
225	1.10	3.55	0.31	1.02
(B) Over 3 days after burn				
205	4.47	8.23	0.54	
210	4.45	7.22	0.61	
196b	5.14	5.57	0.92	

face by absorption into the dressing and evaporation into the air, resulting in a progressive desiccation of the full thickness burn.

When these data on water content are taken into consideration with the sodium content, as shown in Table V, we find that the sodium content (in terms of the weight of tissue water) is normal or increased in eight out of ten full thickness burns. Were the increase in sodium content to be due solely to changes in water content, we would find little or no increase in this figure. The data indicate that when the sodium concentration is expressed in terms of tissue water there is a greater spread than when sodium is referred to tissue weight, and the ratios (of burned to unburned skin) show more departure from unity. This suggests that in some of the cases, sodium may be moving independent of water transfer, whereas in others (cf. Table IV) the differential sodium accumulation is due largely to water loss.

In Table V, the entire series shows a nine per cent increase of sodium content when expressed in relation to the water content of the tissue. In the five cases showing increases, the average is a 27 per cent increase in sodium content as expressed relative to tissue water. It is of interest that these are the same five patients who showed an increase in sodium content when expressed in terms of wet tissue weight. Stated otherwise, when one measures the sodium content and expresses it solely as a function of the total tissue, one finds that there is an increase in sodium content. When this sodium concentration is expressed in terms of the amount of tissue water present, we find that the sodium increase is even more marked, pointing up the fact that the sodium is moving into the tissue in larger quantity than one would predict from the water content alone.

In summary, these data indicate that in the early phase after the burn, both sodium and water are moving into the skin. As the duration of the burn progresses past three days, and approaches a week, the tissue becomes increasingly dehydrated. The sodium that has entered the skin is probably not discharged as rapidly because evaporative water loss leaves the inorganic ions

behind. Therefore, as the skin becomes dehydrated, the sodium content relative to the total tissue water progressively increases.

3. SODIUM EXCHANGE

We now turn to a consideration of the exchange of sodium into the skin from the general circulation. This study was carried out by the use of radioactive sodium injected a few hours prior to the taking of the tissue samples, as described under "Methods".

Under these circumstances, sodium exchange may be studied by comparing the specific activity ratios, (Na^{24}/Na^{23}), of burned to normal skin. If radiosodium alone is determined the results are relatively meaningless as an increased content of Na^{24} may signify only the presence of more total Na^{23} (under equilibrium conditions), rather than any increased *rate* of uptake.

If the specific activity (amount of radioactive sodium per unit of total sodium) of the burned tissue is equal to that of the plasma or the unburned tissue, we may assume that equilibration has taken place and that exchange is complete at the time of sampling. We find in the fresh burns (Table VI), with one exception, that this exchange is complete; in one or two of the cases there is a tendency for a specific activity higher than unburned skin to be observed. The freshly burned tissue may take up sodium so rapidly that when it is sampled a few hours after the injection of the radiosodium, it still shows the high specific activities found in plasma a few minutes after injection, but which have been reduced in the plasma as the sodium equilibrated into other untraumatized tissues. This might be the explanation, for instance, of the specific activity ratio (burned/unburned skin) of 1.14 in patient 240.

Patient 225, (Table VI), showed, though only three days after the burn, practically no radiosodium uptake. This interesting and unusual finding was correlated with the fact that this was a dry flame burn resembling a "char" which doubtless lost its contact with the general circulation much earlier than the other full thickness burns.

From Table VI it is clear that those burns which are studied more than three days after burning tend to show a reduction in radiosodium uptake. This is evidence that the burn has lost contact with the general circulation and cannot enter into physical equilibrium with Na^{24}. Sodium ion is so readily diffusable that if there is any circulatory association whatever between the skin and the plasma, the tissue will rapidly take up the isotope and exchange it for its stable sodium. When this exchange does not take place, it is excellent evidence that the tissue is no longer in contact with the circulation.

4. HISTOCHEMICAL SODIUM SPACE

Table VII shows a series of calculations of the extracellular space of burned skin as based on the sodium and chloride content. This calculation is patterned after that developed by Hastings[9] and simply represents the amount of water in the tissue which contains sodium at the same concentration that it is found in plasma (when corrected for the Gibbs-Donnan effect and the variable water

TABLE VII.—*"Extracellular Space" of Burned Skin.*

As Per cent of Total Tissue Water

$$E_{-} = \frac{\text{Concentration of (x) in wet tissue}}{\text{Concentration of (x) in extracellular water}} \times \frac{100}{\text{Total tissue water}}$$

Concentration of (x) in extracellular water = (x) in plasma adjusted for H_2O content of plasma and extracellular water; corrected for Gibbs-Donnan effect.

Case	E Na Full Thickness	E Na Partial Thickness	E Cl Full Thickness	E Cl Partial Thickness
Number	E Na Unburned	E Na Unburned	E Cl Unburned	E Cl Unburned
A) Under 3 days after burn				
196a	0.83			
254	0.86		1.29	
240	0.97	0.94	1.37	1.29
229	1.09	0.96	1.08	0.87
225	1.18	0.97	1.47	
	0.98 = Mean		1.30 = Mean	
B) Over 3 days after burn				
234	1.10		0.81	
210	1.18		1.10	
231	1.39	1.02	1.29	1.20
205	1.53			
	1.30 = Mean		1.06 = Mean	

Ena was found to be 100% of total tissue water in 6 out of 9 full thickness burns.
Ecl was found to be 100% of total tissue water in 4 out of 6 full thickness burns.

content of plasma and extracellular fluid). This space we called the "Ena." A better term for it possibly is the "histochemical sodium space" emphasizing the fact that it is a tissue measurement of the sodium space made on exactly the same principle that the total radiosodium space is measured in the living patient by studying plasma concentration with relation to injected dose.

If the histochemical sodium space of a full thickness burn (expressed as per cent of tissue water) is the same as the histochemical sodium space of an unburned area of skin from the same patient, one may reasonably assume that the sodium in the burned tissue is still extracellular to the same extent that it is in the unburned tissue. If the histochemical sodium space of a full thickness burn were significantly larger than that of the unburned tissue, one would be forced to conclude either that the extracellular space in the burned tissue was much larger than that of the unburned tissue or that some of the sodium had moved into the cell. If, as a third possibility, the data indicated that the histochemical sodium space approximated 100 per cent of the measured tissue water, one would be forced to the conclusion that sodium had moved into the cells.

In five burns measured under three days after the burn (Table VII), the histochemical sodium space was almost exactly that of the unburned tissue with a mean value for this ratio of 0.98.

After three days, the histochemical sodium space has become expanded and represents approximately a 30 per cent increase over the Ena for normal tissue. In six out of nine of these patients the Ena was equal to 100 per cent of the total tissue water, evidence that sodium has moved into the cell.

This evidence concerning changes in the histochemical sodium space constitutes a chemical demonstration of the fact that full thickness burned tissue, after the third day, is dead tissue though still attached to the organism. Such skin is not exchanging ions with the body fluids of the patient; the normal property of the cell membrane which permits it to exclude sodium from the cellular fluids has been lost, with the result that sodium equilibrates evenly throughout the total tissue water.

5. PROTOCOLS OF TWO PATIENTS

Detailed consideration of two patients, the first a fresh deep burn in the fluid- and sodium-exchange phase, and the second a burn 48 hours after trauma,

TABLE VIII.—*Protocol of Patient 240*

A 5-year-old male child, flame burn of right lower leg from fire in clothing. Excised 4½° after burn, 1° 45′ after Na^{24} injection. Control skin taken from left thigh. No systemic fluid therapy. Burn "parchment-like," little edema, clinically clean. Bacteriology *Staph. albus* and *Alpha strep.* On penicillin.

	Normal Skin	Partial Thickness Burn	Full Thickness Burn	Plasma
H_2O (gm/KG.)	680	682	675	935
Na^{24} (u/Kg.)	737	735	817	1100
Na (mEq/Kg.)	89.6	86.0	86.0	132.6
Specific Activity	8.25	8.55	9.52	8.30
Cl (mEq/Kg.)	45.0	61.2	57.5	101.5
Ena (% Tot. H_2O)	93	87	90	
Ecl (% Tot. H_2O)	61	79	84	

in the "dry-dead" phase, may help in an understanding of the manner in which these data are derived.

In Table VIII (patient 240) are shown the data relative to a full thickness burn in a young child who received his radiosodium injection almost immediately upon arrival at the hospital and who was brought to the hospital very soon after his burn. It was possible to obtain a tissue sample only four and one-half hours after the burn which, in turn, was only one hour and 45 minutes after the injection of radiosodium. This permitted us to make an observation very early in the natural history of the histochemical changes of burned skin.

We find many features characteristic of the early burn. In the first place, the water content of the skin is unchanged. This is to be expected since there has been only a short time in which water content could be increased, there has been little opportunity for the development of edema. Radiosodium uptake, on the other hand, is increased over normal. This is a very delicate measurement of water and sodium exchange and it is apparent that at the time the skin was sampled, it was beginning to demonstrate increased rate of exchange with body fluids as compared with the exchange between normal skin and body fluids. The total sodium content is little changed, again because there has not been time for the accumulation of more total sodium.

The specific activity of the sodium present in this skin is increased about 10 per cent over that of plasma and the other tissues. The explanation of this,

as mentioned before, is to be found in the fact that the specific activity in this skin reflects the high specific activities of plasma an hour or so prior to the time the skin was sampled, at a time when skin was exchanging very rapidly with plasma. Chloride content is somewhat increased, but the Ena and Ecl are not 100 per cent of the total tissue water. They are instead indicative of an extracellular space about normal for skin.

The histochemical description of the skin of this burned child may be summarized by stating that it is a fresh burn which is still in contact with the cir-

TABLE IX.—*Protocol of Patient 225*

A 54-year-old female; epileptic, burned on upper arm by flame during seizure; no systemic fluid therapy. Excised 48 hours later, 1° 20′ after Na^{24} injection. Skin "dead white," considerable edema, clinically clean. Bacteriology *Staph. aureus* and *Staph. albus*. No pre-op. penicillin. Control skin from opposite arm same level.

	Normal Skin	Partial Thickness Burn	Full Thickness Burn	Plasma
H_2O (gm/Kg.)	730	810	790	935
Na^{24} (u/Kg.)	335	373	121	481
Na (mEq/Kg.)	96	103	117	135
Specific Activity	3.55	3.64	1.10	3.57
Cl (mEq/Kg.)	64.0		91.7	108.0
Ena (% Tot. H_2O)	91.3	88.6	100.8	
Ecl (% Tot. H_2O)	72.0		108.0	

culation, it is exchanging sodium, and presumably chloride, more rapidly than is the normal skin in the same patient; there has not yet elapsed enough time since the burn for either water or total sodium to accumulate in the tissue and, lastly, that sodium and chloride are still confining themselves to the extracellular phase of the tissue and have not moved into the cell.

In contrast are the data on patient 225 (Table IX), the patient previously mentioned in whom a full thickness burn was associated with very little radiosodium uptake at 48 hours. It will be noted that this burn, excised 48 hours after the trauma, showed some increase in water content, a finding which probably was traceable to the fact that in the first 24 hours after the burn the skin was capable of accumulating measurable edema. The radiosodium uptake, on the other hand, is greatly diminished, as compared with normal skin or partial thickness burned skin taken from the same patient. The total sodium content in terms of mEq/Kg. of total tissue (wet weight) shows an increase over the normal skin. Again this is to be interpreted as evidence of the fact that sometime during the 48 hours which preceded radiosodium injection and excision, this skin had taken up both water and sodium in greater quantities than the normal skin in the same patient. The specific activity of the sodium in this burned skin (the ratio of Na^{24} to Na^{23}) is therefore less than that observed in normal skin from the same patient, by 30 per cent. It is also of interest that the specific activity of the normal skin, the partial thickness burned skin, and the plasma in this patient are all in equilibrium by the time of biopsy. Since these figures for specific activity (Na^{24}/Na^{23}) are derived from measures both

of radioactivity and total sodium in the tissue, they constitute a check on the accuracy of the methods. The specific activity ratios for these various normal tissues should come to unity with a readily diffusable ion one hour and twenty minutes after injection, as the observed values indicate.

The chloride content of this full thickness burned skin was increased. The

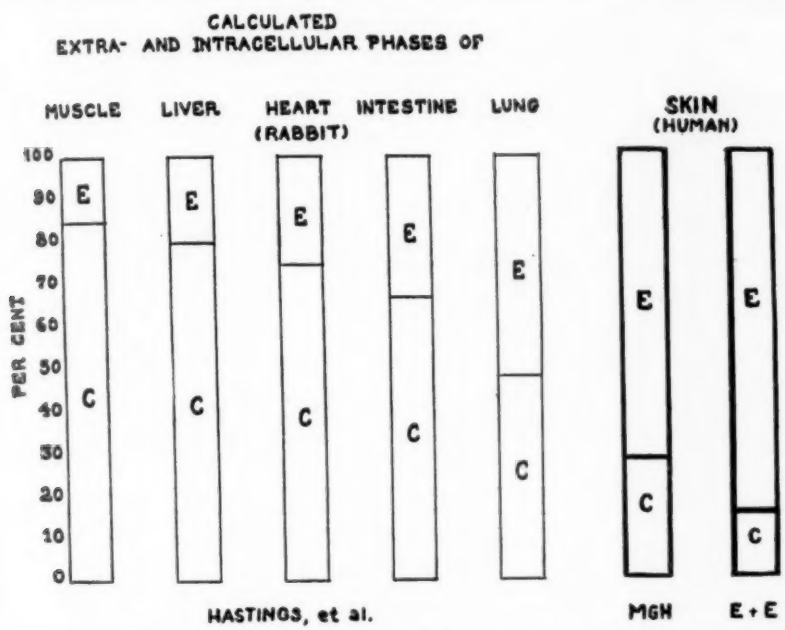


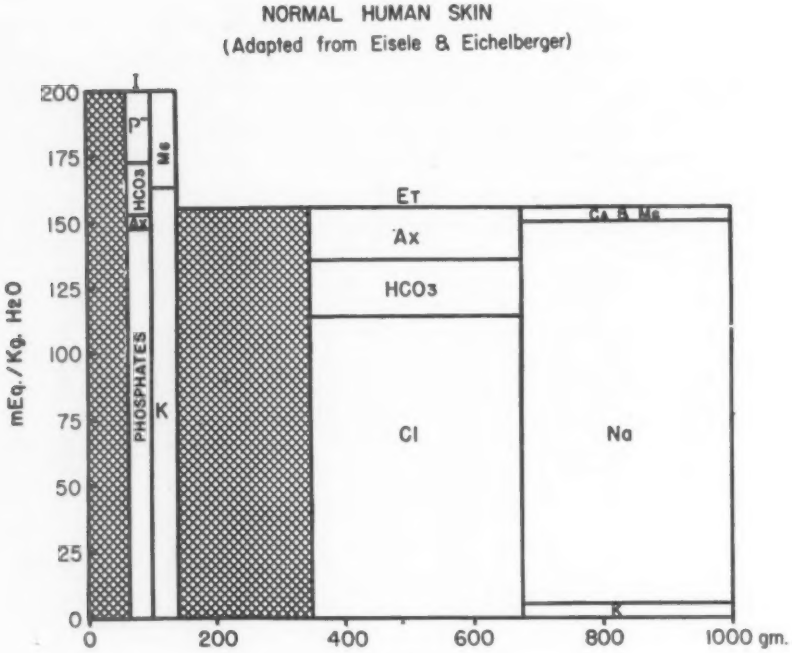
CHART I.—Diagrammatic representation of the relative intracellular and extracellular phases of various tissues. The extracellular phase is indicated by the letter "E," the intracellular phase by the letter "C." The rabbit data are those investigated by Hastings, et al., the human data are those reported herein ("MGH") and by Eisele and Eichelberger ("E&E").

Ena and Ecl both were increased and in the full thickness burned skin represented approximately 100 per cent of the total tissue water.

The data, then, allow us to characterize the burned skin from this patient as being skin which, sometime in its first 48 hours, took up water, sodium, and chloride but which, since that time, has lost its contact with the general circulation so that it is no longer exchanging ions with the plasma. The sodium and chloride in the skin have moved into the cell at essentially the same concentration at which they are found in the extracellular fluid.

DISCUSSION

An examination of histochemical concepts as applied to skin will aid us in an understanding of these data as well as the significance of possible sodium-potassium exchange in the cells of muscle after trauma. It must be emphasized that the great soft tissue mass of the body consists of striated muscle and that the skeletal muscles contain more protoplasmic protein than any other single tissue. When muscle, liver, kidney, lungs and heart are considered together,



Total H_2O	= 718.0	Gm/Kg	wet	tissue	
$(H_2O)_E$ (Na)	= 638.0	"	"	"	"
$(H_2O)_C$	= 80.0	"	"	"	"
$(H_2O)_E$ (Cl)	= 690.0	"	"	"	"
Na	= 93.0	mEq/Kg		"	"
Cl	= 79.9	"	"	"	"
K	= 16.47	"	"	"	"
C.T.	= 216.0	Gm/Kg		"	"

CHART II.—Histochemical diagram of normal human skin. In this and the subsequent three charts, the horizontal coordinate is drawn in proportion to the weight of wet tissue, the vertical coordinate representing the concentration of solutes in tissue water. The symbol "E_t" indicates extracellular tissue whereas the symbol "I" represents intracellular tissue. The relative concentration of anions and cations is shown in the two open columns within each tissue phase. The designation of the coordinates is such that the area within a subcompartment of the diagram is roughly proportional to the total weight of solutes present. A_x indicates organic anions. The cross-hatched area represents non-ionized solids; in the case of extracellular tissue, this is largely collagen, elastin and other connective tissues and, in the intracellular phase, structure proteins.

Beneath the chart are shown some calculations of the quantities of water and solutes present. "$(H_2O)E(NA)$" indicates the volume of extracellular water found by sodium analysis; "$(H_2O)E(Cl)$" the same entity by chloride analysis. ("$H_2O'C$" represents intracellular water (by difference). "C.T." signifies connective tissue. These data are derived from the work of Eisele and Eichelberger.

one has accounted for 95 per cent of the protein-containing cellular tissues of the body. No matter what their order of magnitude, it would be unlikely that histochemical changes in skin alone would be responsible for more than minor shifts of water and electrolyte, in terms of the total organism.

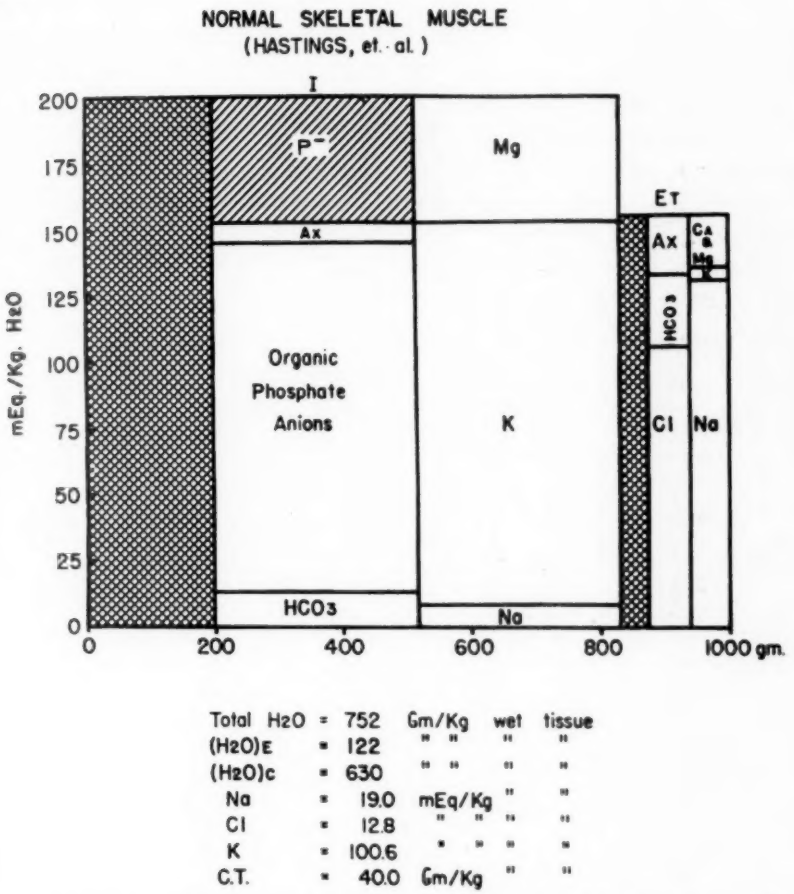


CHART III.—Histochemical diagram of normal skeletal muscle (Hastings). The method of depiction and the symbols used are the same as in Chart II. "P-" represents the equivalence of protein as anion.

An additional consideration has to do with the relative extracellular and intracellular compartments of skin as contrasted with other tissues of the body. In Chart I is shown a series of columns representing the division between extracellular and intracellular phases of tissues based on the determinations of Hastings,[13] and to this has been added the data on skin from our laboratory and from the work of Eisele and Eichelberger.[10] It will be seen from reference to this diagram that in skin the extracellular space dominates the tissue and that only a small compartment is within the cell. Histologic examination of dermis and epidermis, of course, corroborates this chemical determination in that the cellular layer is only 30 to 80 micra thick whereas the whole dermis may extend for four or five times that depth, the dermis being relatively cell-free. The calculations of extracellular space shown in Chart I are based on chloride and sodium analyses. It will be observed that muscle, liver and heart are all highly cellular tissues, quite removed from skin in their composition. There are few tissues of the body which contain less cellular material than skin and

these include such tissues as tendon and cartilage, tissues which are also relatively rich in sodium. Therefore, if one is considering exchange of ions between the cell and the extracellular compartment, it is quite apparent that muscle, liver or heart are much more capable of producing massive shifts of this variety than skin or other tissues low in cellular content.

In Chart II is shown a more detailed diagram of normal human skin based upon the data from Eisele and Eichelberger,[10] who made determinations of total connective tissue volume, which were not made in our series. It is again quite evident that over 80 per cent of the tissue is extracellular and that the sodium concentration is quite high in the tissue as a whole. Therefore, release

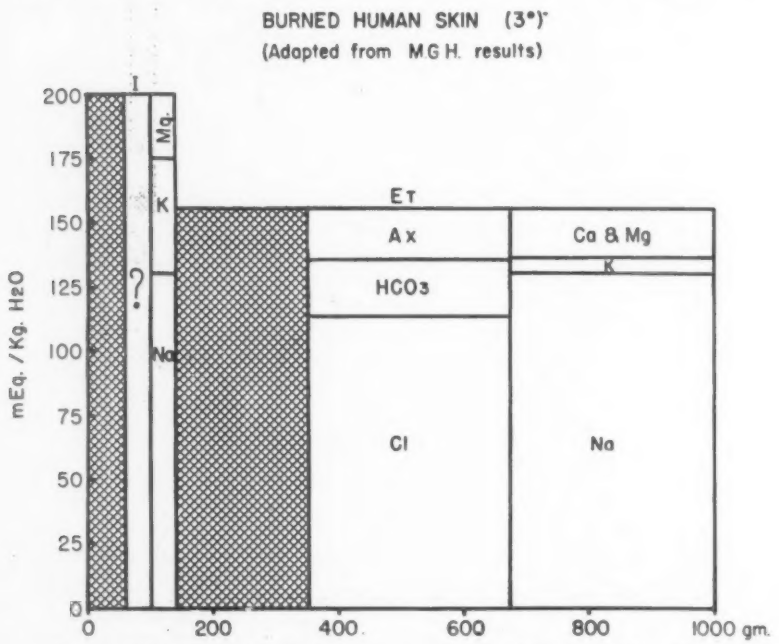


CHART IV.—Histochemical diagram of burned human skin. This chart is based on work reported herein; the chemical structure is still fragmentary. We have little evidence as to changes in intracellular anions. Sodium-potassium exchange is minimal despite the (relatively) great change in intracellular sodium.

of potassium from the cell or loss of sodium into the cell will inevitably be of minor importance relative to the organism as a whole.

In contrast to this is shown in Chart III an histochemical diagram of normal skeletal muscle. It is apparent that the tissue is over 80 per cent intracellular and that there is maximal opportunity for sodium-potassium exchange.

In Chart IV is shown a diagram of what might ensue in burned human skin were sodium and potassium to exchange in such a way that the intracellular sodium concentration were the same as that in the extracellular fluids. It is of interest that this theoretical calculation, (based on data from Eisele and Eichelberger,[10] and from Hastings[13]) indicates that skin would permit an

approximately 15 per cent increase in sodium content computed on the basis of total wet tissue. This is the same magnitude we have observed following burns, constituting another indirect evidence that the sodium shifts described in burned patients probably indicate the entrance of sodium into cells.

On the basis of the quantities shown in Chart IV, one may carry out approximate calculations indicating the deficit this "sodium loss into the cell" would create in the body as a whole if skin alone were involved. In a 70-kg man of average height and assuming a 50 per cent burn, approximately four and one-half kilograms of skin would be burned as a maximum. This would impose a sodium deficit on the patient of only 35 mEq, which could be sup-

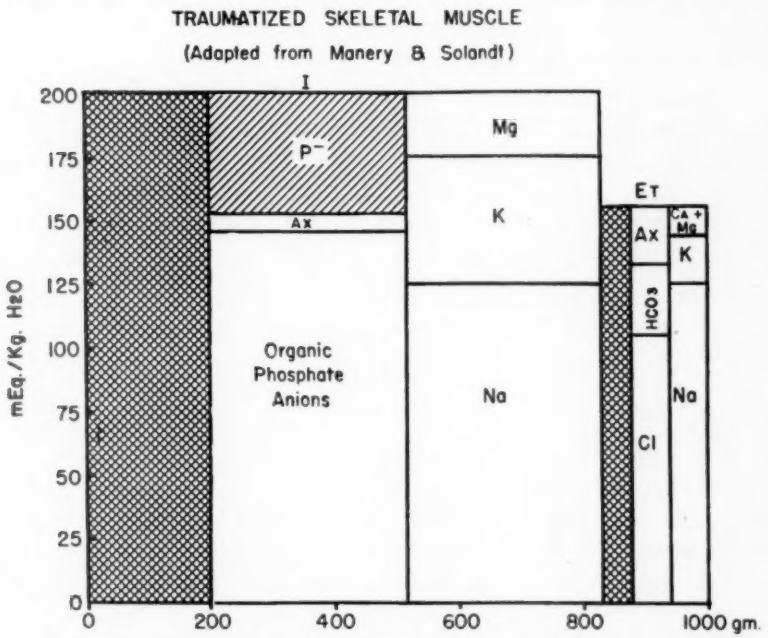


CHART V.—Histochemical diagram of traumatized skeletal muscle. This is based on the work of Manery and Solandt; the mass of sodium and potassium exchanged is very large, due to the relatively large size of the intracellular compartment.

plied by only 450 cc. of normal sodium solution, an amout which is approximately one-twentieth of that usually required in the first 24 hours of a burned patient's treatment.

The potassium release from this skin would theoretically total 35 mEq, and with an extracellular volume of 20 liters, this would increase the potassium concentration only 1.9 mEq/L, assuming that there is no excretion.*

In contrast to this situation, in Chart V are shown the chemical events which would ensue were 10 Kg. of muscle mass to be so traumatized that

* The excretion is, in fact, increased during such situations and potassium concentration in the plasma has not been observed as significantly increased in our experience with burned patients.

sodium-potassium exchange could occur. Such an event might consist of trauma involving ischemia to the muscle, or some such injury as a crush. One may calculate the potential sodium-potassium exchange involved in such muscle trauma; the changes would present the body with a sodium deficit of about 640 mEq which would require almost five liters of normal saline to satisfy, and the potassium release would be so massive as to increase the potassium concentration to toxic levels (15 mEq/L or higher), providing renal function did not take care of this excess.

SUMMARY AND CONCLUSIONS

1. The histochemical changes in burned human skin are described.

2. The established histochemistry of skin and muscle are contrasted with respect to their potential for cation transfer.

3. From these data, observed and calculated, we may conclude that, following burns, the entrance of sodium into skin cells is evidence of cell death; it is an alteration in tissue chemistry of great local significance. From the viewpoint of the total organism, however, such alterations impose little sodium deficit and no discernible potassium excess.

4. Were similar changes to occur in skeletal muscle, massive electrolyte transfer would seriously alter the chemical composition of both intracellular and extracellular fluid, and endanger survival.

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POLYPOID ADENOMATOSIS OF THE ENTIRE GASTRO-INTESTINAL TRACT *

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THE CHILD WHOSE HISTORY is the basis of this report presented a remarkably interesting and confusing clinical picture which was finally elucidated only by autopsy.

Case 1.—R. T., A-44010. The patient was a white male infant, first admitted to the Harriet Lane Home in October 1945 at the age of 10 months. He had been born by breech delivery after a difficult labor and had been cyanotic for the first four days of life. From birth he had suffered from diarrhea with numerous large, foul stools—up to twelve daily. Despite a good appetite and ample food intake he failed to gain weight, and it was observed that food passed unchanged in the feces. He had coughed almost from birth and at the age of nine months had been treated elsewhere for "bronchopneumonia." In the succeeding month he had lost five pounds in weight and had become weak and pale.

On physical examination the child presented a picture of advanced malnutrition and cachexia. He was pale, weak and lethargic, and coughed frequently. He weighed only 7500 Gm., had only 2 teeth, could not walk, crawl, or sit up, and was scarcely able to hold up his head. There were generalized inspiratory rales and the liver and spleen were enlarged. It was thought, with the diarrhea, malnutrition, and chronic pulmonary disease, that the child had cystic fibrosis of the pancreas, but the duodenal enzyme studies failed to support the diagnosis. When the child was placed on a metabolism bed to permit studies of stool fat, he had a rectal prolapse (Fig. 1), exposing many polypoid tumors on the rectal mucosa, some almost 2 cm. in diameter.

An ordinary gastro-intestinal series and barium enema failed to show any lesion. There was "chronic non-tuberculous infiltration" of the lungs on roentgenographic examination and bronchoscopy revealed diffuse bronchial inflammation with purulent secretions. A second barium enema finally showed numerous polyps (Fig. 2) in the colon. Rectal prolapse became a chronic recurrent condition until the polyps were removed with the cautery loop. Roentgenograms were made by introduction of barium through a Miller-Abbott tube which had been passed into the small intestine. No polyps were seen.

Considerably improved by numerous blood transfusions, the child was discharged. It was thought that he had polypoid adenomatosis of the colon and it was felt that colectomy would be required for relief. He was to be followed in the out-patient department pending the result of experimental investigation of the feasibility of total colectomy and anal ileostomy with preservation of the sphincter. Sigmoidoscopy of the mother and of the putative father showed no polyps in the rectum of either and neither had any suggestive symptoms.

In February 1946, three weeks after discharge, he was readmitted because of a mild balanitis. Rectal prolapses of major proportions recurred frequently and diarrhea had continued. His condition aside from the balanitis did not change during the two weeks of this admission.

In May 1946, when he was 18 months old, he was admitted to the Harriet Lane Home for the third and last time. The rectum had prolapsed on four more occasions and he continued to have three to seven loose, bloody stools a day. Edema of the legs had increased progressively for three weeks. He now weighed only 8600 Gm. and appeared cachectic with progeric facies. There was generalized edema and the clubbing of the fingers and toes, which had developed during the first admission, was more prominent than before.

* Submitted for publication, July, 1948.

He still had a constant cough and the fine rales were still present throughout both lungs. The hemoglobin was 10.5 Gm. The total serum protein was 3.33 Gm. per cent, albumin 2.34 Gm. per cent, globulin 0.99 Gm. per cent, with an A/G ratio of 2.36. Numerous other blood chemical determinations gave results within the normal range. Again the pancreatic enzyme studies gave results in the normal range. The lungs were clear on roentgenographic examination. He was transfused repeatedly. On May 29, 1946, he began to have obvious abdominal pain, and after about 18 hours a mass was felt in the left

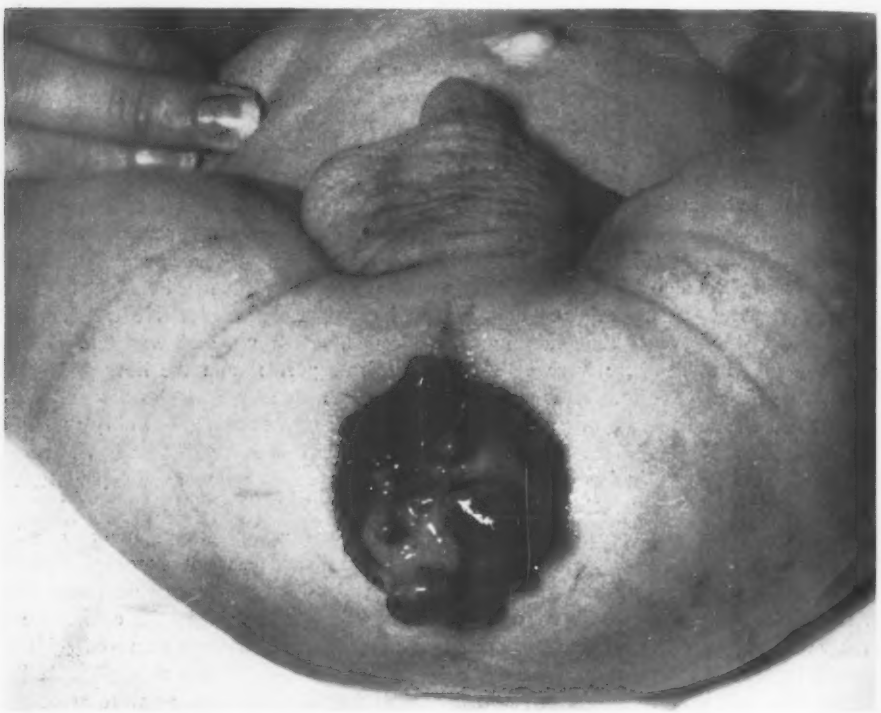


FIG. 1.—R. T., age 11 months.—Rectal prolapse showing numerous adenomata of considerable size.

lower abdomen; he became distended and vomited, and the diagnosis of intussusception was made.

At operation (Dr. W. E. Grose) there was found a bluish discolored intussusception a foot long, involving the ileum and reaching almost to the ileocecal valve. The intussusception was rapidly resected and an end-to-end anastomosis performed. Many polyps were felt in the small bowel well above the intussusception. The resected bowel was gangrenous and showed numerous polypoid adenomata, many of them large and pedunculated. The child tolerated the procedure surprisingly well, but had progressive difficulty with respiration and died 24 hours after operation.

Autopsy 19978, May 31, 1946. The entire intestinal tract from the cardia of the stomach to the anus was involved in a remarkable process. Every segment was affected and no areas were "skipped." The mucosa was covered with innumerable polypoid tumors, the character and distribution of which varied from segment to segment. The stomach (Fig. 3) was the seat of a great number of polyps, most of them large, measuring one to several centimeters in diameter, usually sessile but occasionally pedunculated. There were numerous smaller pedunculated duodenal polyps. (Fig. 4.) The entire jejunum and

ileum were spotted with polyps, as shown in the photographs. (Fig. 5.) The anastomosis had been performed a few centimeters above the ileocecal valve and appeared to leak after the adherent bowel had been separated at autopsy. It was felt that in life an adjacent loop had sealed the leak. The colon (Fig. 5) was carpeted with polyps, large and small,

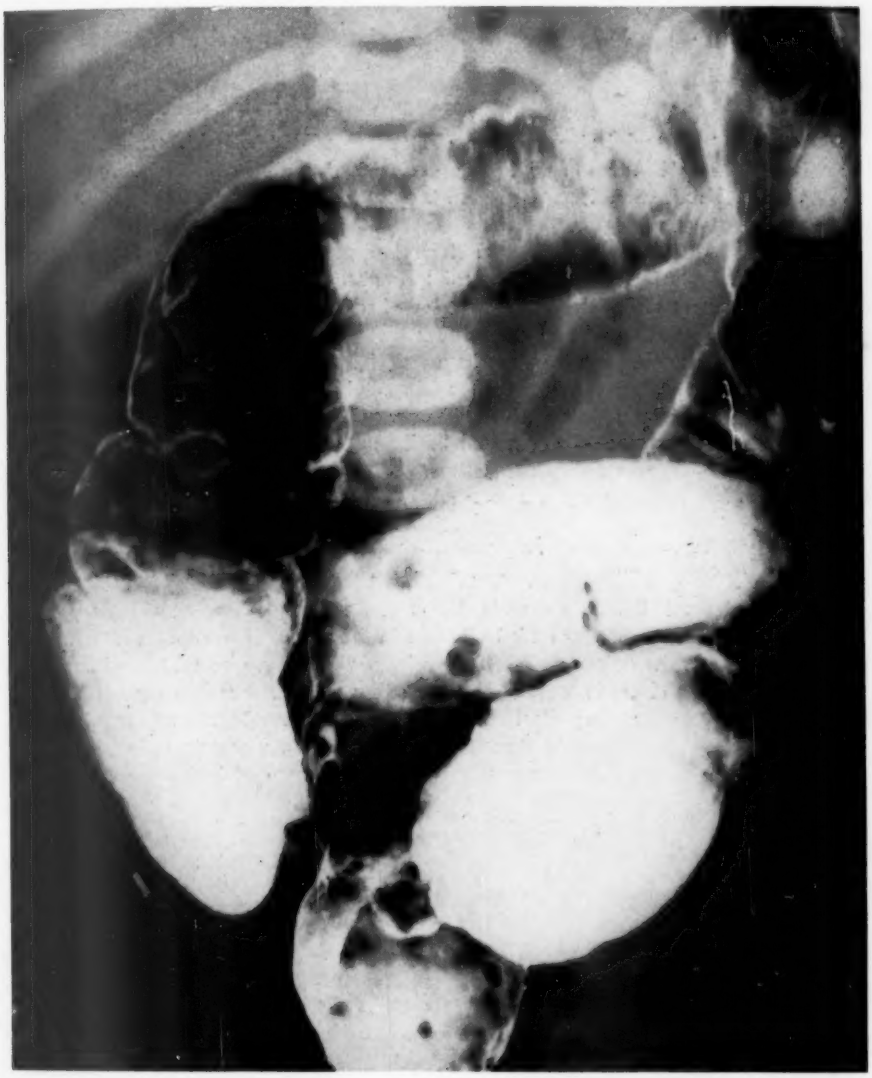


FIG. 2.—R. T., age 11 mos. Barium enema.—Numerous round radiolucent areas are seen in both right and left colon. As seen in Fig. 5, the bowel was literally carpeted with adenomata. Only a few tumors are revealed by the barium enema.

sessile and pedunculated, for its entire length. The terminal 10 cm. of the rectum, in which the polyps had been fulgurated months before in an attempt to prevent repeated rectal prolapse, now showed only small polyps. The pancreas was normal. There was emphysema and patchy atelectasis of the lungs. The child had the hippocratic osteo-arthropathy of fingers and toes which had been recognized in life. No other disease was

FIG. 3.

FIG. 4.

FIG. 3.—R. T., age 18 mos. Autopsy specimen of stomach.—There are numerous polypoid tumors, most of them large (up to 3 cms. diameter) and many of them ulcerated.

FIG. 4.—R. T., age 18 mos. Autopsy specimen.—Duodenum with attached segment of liver. There are many adenomata, mostly pedunculated, and much smaller than those in the stomach.

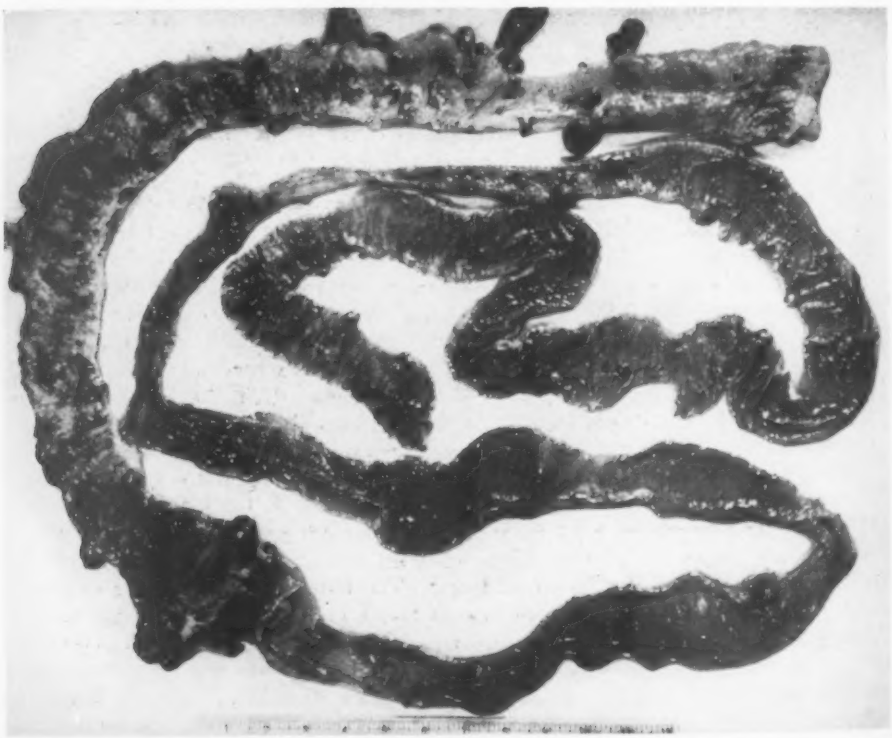


FIG. 5.—R. T., age 18 mos. Autopsy specimen.—Every segment of the small bowel is spotted by great numbers of tumors. The large bowel is even more heavily seeded and the tumors tend to be larger. In the last few inches of rectum and anal canal the adenomata, though numerous, are very small due to the previous electrosurgical section. The end-to-end anastomosis is just proximal to the cecum.

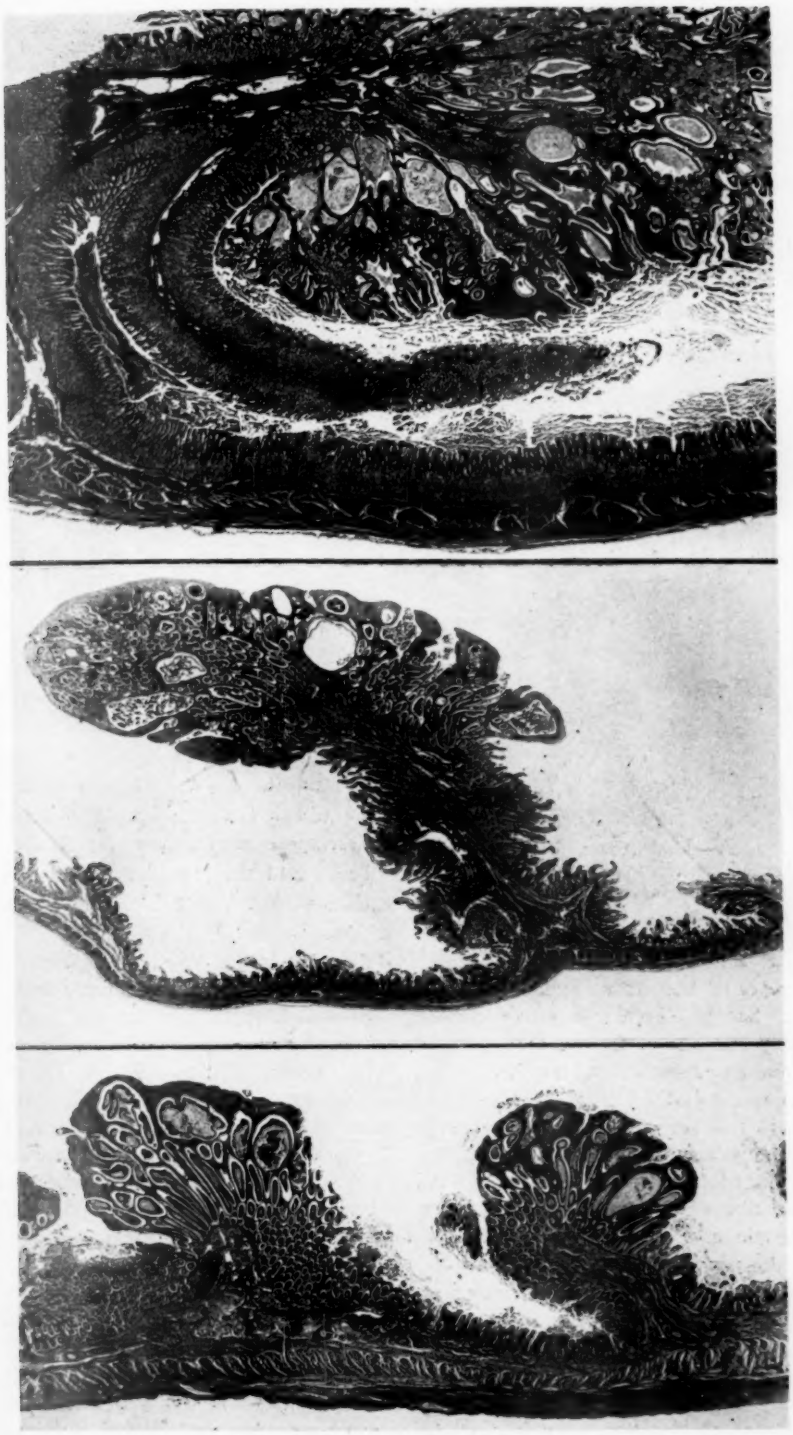


FIG. 6.—Photomicrographs of tumors of R. T.—A. Section of gastric polyp x 10. The tumor is a true polypoid adenoma, being composed entirely of a mass of glands. B. Jejunal tumor x 10. This tumor is more pedunculated and the fibrous stroma has been pulled out into the base. C. Section of the colon x 10 showing that the polyps are almost contiguous.

found, but the diffuse gastro-intestinal adenomatosis. Sections of the polyps presented the usual picture of true adenomata, as illustrated in the photomicrographs. (Fig. 6.)

A second patient was seen recently on the private service of Dr. I. R. Trimble. At operation she was shown to have polyps of the stomach and of several segments of the small bowel. Rectal polyps were visible through the sigmoidoscope. The precise degree of involvement in her case can not as yet be stated with certainty.

Case 2.—J. E., 439670. A white girl, aged 16 years, was first seen in this hospital in 1937 at the age of six. At that time she was being studied for severe chronic secondary anemia with bloody stools and repeated attacks of abdominal pain with audible peristaltic rushes. While on the ward and before a diagnosis had been made, an obvious intussusception developed. Abdominal exploration by Dr. I. R. Trimble revealed two separate intussusceptions of the small intestine, one associated with a single polyp and the other with two polyps. These intussusceptions were rather far apart, one being in the mid-ileum, the other in the terminal ileum. The intussusceptions were reduced and the polyps excised. Convalescence was uneventful.

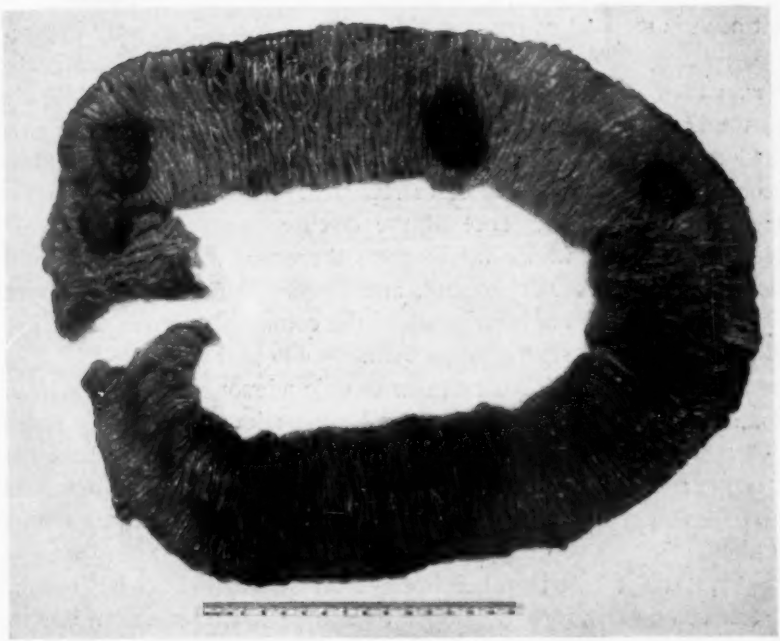
FIG. 7.—J. E., age 16 years. The pigmented patches on upper and lower lip are plainly seen. Others are within the mouth.

The child had been noticed almost from birth to have peculiar brown pigmented spots on the vermilion portion of her lips and on the adjacent mucous membrane (Fig. 7). The significance of these was first appreciated on the present admission because of the previous clinical observations of Dr. Victor McKusick in similar cases.[17]

After her operation she remained well until 2 or 3 years before the present admission, when repeated attacks of abdominal pain began, accompanied by a chronic secondary anemia. She had been taking iron constantly by mouth so that it was not possible to draw any conclusions from the color of her stools. There had never been any massive hemorrhage and she had never had diarrhea, tending rather to be constipated. The attacks of pain might last as long as 24 to 36 hours with cramps one or two minutes apart. No attack had been as severe as the one for which operation had been performed. However, during one particularly severe attack 2 years before her present admission she was operated upon in her home community and obstructing bands of adhesions were divided. She was occasionally nauseated with her attacks, but vomiting was rare. Sigmoidoscopic examination and repeated roentgen studies of the entire gastro-intestinal tract were negative.

On physical examination she was seen to be a bright, alert girl of 16, thin and very pale. There were numerous peculiar irregularly-shaped flecks of brown pigment on the lips and oral mucosa, varying in size from 1 to 2 or 3 mm. in diameter. (Fig. 7.) There was no definite clubbing of the fingers or toes, although the distal phalanges of the fingers were suggestively spatulate. The abdomen was scaphoid. There was a well healed lower midline scar. No masses were felt and there was no tenderness. Digital rectal examination was negative. Laboratory tests: hemoglobin 8.2 Gm., red blood cells 3.39 million.

A



B

FIG. 8.—J. E., age 16 years.—A Photomicrograph x 10 of one of two polypoid tumors removed from stomach by gastrotomy. B. Segment of jejunum resected at second operation and containing 6 large polypoid adenomata. This patient had rectal tumors seen through the sigmoidoscope.

total serum proteins, 5.9 Gm. per cent, stools—positive guaiac test for occult blood, urine negative.

On sigmoidoscopy two small rectal polyps were seen within 10 cm. of the anus. Repeated roentgenographic studies of colon, stomach, and small intestine, the latter being made with barium introduced through an indwelling tube, all failed to show polyps.

After repeated transfusions of whole blood, on October 31, 1947 operation was performed by Dr. Trimble. Two separate large polyps 1.5 cm. in diameter were palpable in the stomach and were removed by gastrotomy. (Fig. 8a.) A segment of jejunum about 100 cm. long was found to contain eight large pedunculated polyps, the largest being 2.5 cm. in diameter. This segment of bowel was resected (Fig. 8b) and an end-to-end anastomosis performed. Recovery from operation was smooth, and the child was discharged on November 25, 1947, much improved.

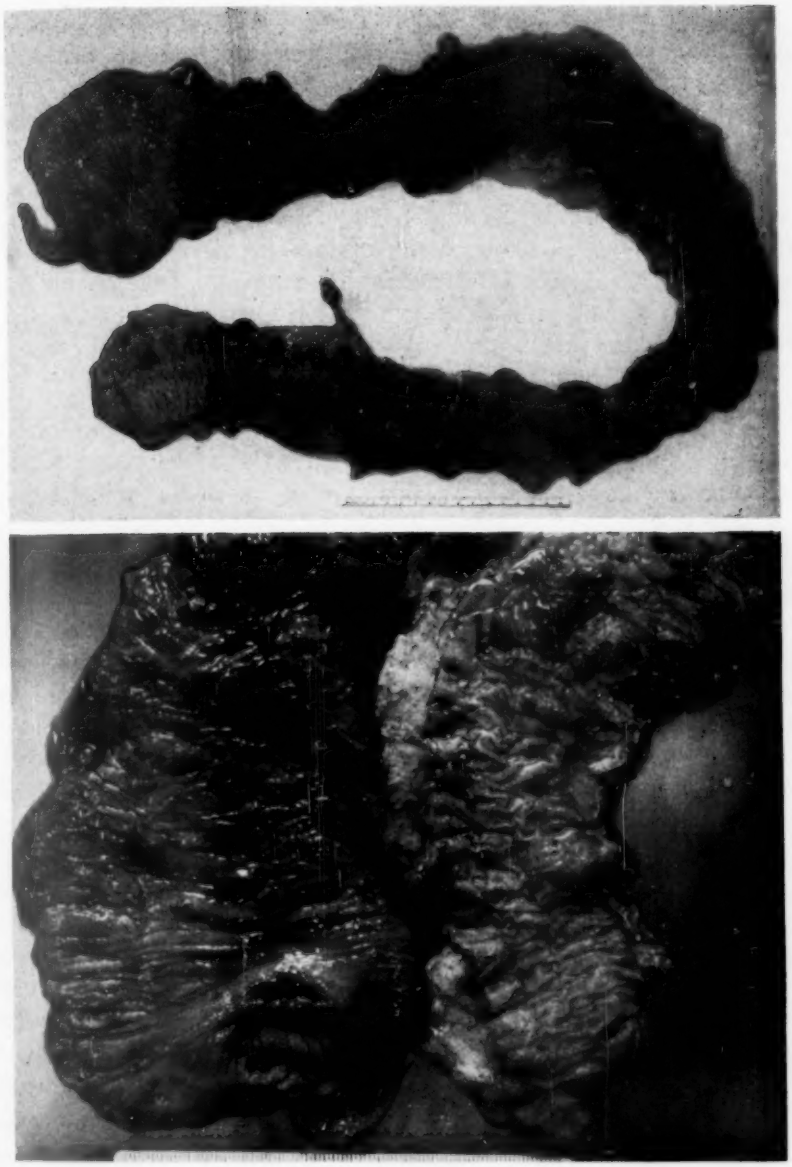
POLYPOID ADENOMATOSIS OF THE COLON

The literature on polypoid adenomatosis is confused by the inclusion under this heading of many patients with only a few, six or eight, polyps of the colon. Such patients have multiple polyps, indeed, but not polypoid adenomatosis. Their disease is not familial, the prognosis is more favorable, and the required treatment less radical since removal of the individual tumors is adequate treatment. In true polypoid adenomatosis the entire colon, or a large segment of it, is the seat of innumerable polyps. The polyps vary in size from those just barely visible to the naked eye to those several centimeters in diameter, either sessile or pedunculated. Under the heading of "polyposis coli" in the literature are found many reports of the condition more properly described as familial polypoid adenomatosis of the colon. There have by now been several hundred such cases reported. Since Cripps' original observation[2] of the familial incidence of the disease, many instances have been reported of patients in whose family trees there was a high incidence of this condition.[3, 4, 5] Bensaude, Hillemand, and Augier[6] have reported several patients in whom polypoid adenomatosis of the colon was accompanied by clubbing of the fingers and sexual infantilism.

The feature of prime importance in colonic adenomatosis is the inevitable development of cancer in one or several such adenomata. It is repeatedly stated[7, 8] that all patients with polypoid adenomatosis will ultimately have cancer of the rectum, if they survive long enough, and the incidence of cancer in various series, as of the time of the given report, has been as high as 43 per cent.[9]

The diagnosis is based on the history, on digital and visual examination of the rectum, upon a properly performed double contrast barium enema, and lastly by operation. It has been our experience that the barium enema may demonstrate only a few of the larger polyps, as can be seen by comparing the picture of the specimen of R. T. (Fig. 5) with the roentgenogram (Fig. 2) of the same patient. It is noteworthy, furthermore, that polyps may be excessively difficult to palpate at laparotomy, as exemplified by a 25-year-old man who was seen recently. His mother had polypoid adenomatosis with three separate carcinomas of the left colon, and his three sisters all had bloody diarrhea and typical sigmoidoscopic findings. Multiple minute polyps and one larger polyp

A



B

FIG. 9.—B. McG., age 26.—Specimen removed at first operation. A. Entire specimen. Numerous larger adenomata are seen. The smaller ones, as in the cecum, are almost invisible. B. Close-up of cecum (left) and rectum (right). Note the great number of very small mucosal tumors. It was impossible to feel these at the time of operation.

about 0.5 cm. in diameter were found on sigmoidoscopy of the patient but barium enemata were equivocal. At laparotomy careful palpation revealed only one polyp in the entire colon, and that one on the left side, probably the one seen through the sigmoidoscope. Nevertheless, it was felt that he must have polypoid adenomatosis, and a total colectomy was begun, in this first stage resecting the colon from the ileocecal valve to the rectum. The specimen (Fig. 9) showed the bowel carpeted with polyps for the length of the specimen.

The treatment advocated is indicated above—total colectomy with a permanent ileostomy, preferably anal as recently reported.[10] Several authors have reported successes with subtotal colectomy and repeated fulguration of the rectum. This is a dangerous half measure. The mucosa of the remaining segment retains its genetic predisposition to polyp formation with the ultimate risk of cancer. There are a number of reports of cancer developing in the preserved rectal segment and we have seen this occur once[10] after such a procedure.

POLYPOID ADENOMATOSIS OF THE SMALL INTESTINE

Adenomatosis of the small intestine is different in many respects from familial adenomatosis of the colon. It has only occasionally appeared to be familial. Reisinger[11] operated upon a father and a daughter for repeated intussusceptions due to multiple jejunal polyps. Malignant degeneration has occurred[12, 13, 14] but is uncommon. Adenomatosis of the small intestine is apt to manifest itself by repeated bouts of abdominal discomfort, sometimes vague, sometimes exceedingly acute. These attacks apparently indicate intestinal obstruction due either to the polyps themselves or to associated intussusceptions. The most characteristic feature in the histories of reported cases is the frequency of repeated operations for intussusception. Gatersleben[13] cites four patients with multiple polyps of the small intestine who had together been operated upon for intussusception on ten different occasions.

Diagnosis has been very difficult and is rarely made before operation, which is generally undertaken for an attack of acute intestinal obstruction due to intussusception. Raiford[15] stated that 23 per cent of patients with benign tumors of the small intestine had intussusception. In several instances we have attempted roentgenography unsuccessfully by a double contrast method, introducing the barium and air into the bowel through an indwelling tube passed to the small intestine. Jeghers[16] and McKusick[17] have individually rediscovered and remarked upon Hutchinson's observation of peculiar pigmentation of the buccal mucosa in some patients who subsequently proved to have polyps of the small or large intestine, as in the second patient described in the present report.

The treatment of polypoid adenomatosis of the small bowel depends on the extent of the disease. The jejunum is apparently the segment of the small intestine most commonly affected by large numbers of polyps (Beales,[18] Struthers,[12] Shaw,[19] Atakam,[20] Björkroth[21]). It is much more rare to find the entire small intestine involved in polypoid disease (Reisinger,[11] Manfredi[22]). If all

the polyps occur in one segment of small intestine it is probably worth-while to resect that segment. Elective resection is hardly warranted if the polyps are scattered through the entire length of the small bowel or if there are polyps in the colon (Niemack[23]) or in the stomach (Wechselman[24]). In such instances one adopts a more or less passive attitude. Operation is performed only when demanded by the occurrence of an intusssusception, and then the segment involved should be resected rather than reduced and left behind.

POLYPOID ADENOMATOSIS OF THE STOMACH

Polyps of the stomach, even when multiple and covering most of the stomach, may be peculiarly silent. Pearl and Brunn[25] reported 125 collected cases, in which they found no evidence of familial incidence. Of the 37 patients most recently reported, cancer had developed in 19 by the time of the report. Pearl mentions the well-known difficulty of demonstrating gastric polyps roentgenographically. It has frequently been reported that stomachs which are the seat of numerous polyps have appeared normal in the gastro-intestinal series. The roentgenograms of R. T. failed to demonstrate the innumerable polyps (Fig. 3) in the stomach. Polyps may cause vague malaise, indigestion, melena, or hematemesis, or a large polyp occluding the pylorus may at times produce intermittent obstructive symptoms.

Radical gastrectomy is the treatment of choice for gastric adenomatosis (Pearl and Brunn,[25] Kaarstad[26]) not associated with adenomatosis of other portions of the intestinal tract. The likelihood of malignant degeneration is at least as high as it is in polypoid adenomatosis of the colon. In the absence of any obvious genetic factor it is probably not necessary to perform total gastrectomy, provided no polyps are seen by direct inspection of the mucosa of any portion of the stomach which can be left behind. In the stomach, even more than in the small or large intestine, palpation through the thick bowel wall cannot be relied upon to reveal polyps, and if they are suspected and not felt, gastrotomy must be resorted to before it is safe to state that the stomach is free of polyps. The incidence of gastric polyposis associated with colonic or rectal polyposis is too high to be accidental (Gejrot,[27] Wechselman,[24] Port,[28] Schöttler[29]). The occurrence of these potentially malignant lesions at both ends of the gastro-intestinal tract poses a difficult surgical problem.

POLYPOID ADENOMATOSIS OF THE ENTIRE GASTRO-INTESTINAL TRACT

The patient presented first in this report aroused our interest because of the simultaneous occurrence of polypoid adenomatosis in several segments of the intestinal tract. The number of instances reported is not large and only two substantiated similar instances have been found of adenomata carpeting the intestinal tract from the cardia to the anus. There were ten additional reported cases in which each segment of the intestinal tract, beginning with the stomach, had at least a few polyps.

Glass[30] reported two instances of diffuse polypoid adenomatosis of the gastro-intestinal tract. The most striking case was a female patient who was followed for 19 years. From the age of 12 she had had postprandial cramps

and vomiting and had been thought to have a duodenal ulcer. In 1918, when she was 20, Dr. Charles Mayo operated upon her for a three-day attack of intestinal obstruction and removed four duodenal polyps. In 1919 she was operated upon for an intussusception of the ileum and three feet of bowel were resected, containing many polyps "as large as a lime." She remained well until 1928 when another intussusception was reduced and four polyps were removed. In 1929 she was operated upon for rectal bleeding and one large sigmoid polyp, three rectal polyps, and one cecal polyp were removed. In 1930 Dr. Fred Rankin performed a left colectomy. In 1935 she was acutely ill at the Memorial Hospital in New York, under the care of Dr. George T. Pack. The stomach was found to be filled with polypoid masses and resection was considered inadvisable. Autopsy disclosed generalized gastro-intestinal polyposis.

The other patient reported by Glass was a male of 27 with symptoms of hematemesis and melena who was found on roentgenography to have polyposis of the entire gastro-intestinal tract. Further details are not given.

The best substantiated report of polypoid adenomatosis involving all of the gastro-intestinal tract was that of Brachetto-Brian and Lascano[31] who reported the case of a 53-year-old female with vomiting, tenesmus, and bloody diarrhea of one week's duration and a palpable mass on rectal examination. She died after resection of the rectum for carcinoma. At autopsy the stomach was found to be covered with large polyps, sessile and pedunculated, and the entire small intestine was covered with polyps, with multiple but fewer discrete larger polyps in the colon. The sigmoid tumor measured 5 by 6 cm. and was frankly malignant.

Petrow's [32] is one of the earliest reports. His patient, a 26-year-old female, was operated upon for a gangrenous ileocecal intussusception of 15 days' duration and died. There were multiple gastric polyps, pedunculated duodenal polyps, and multiple polyps of the remainder of the gastro-intestinal tract. The title of the report indicates malignant degeneration of one of the polyps. The original article has not been available for the present report.

Shaw,[19] in reporting five cases of polyposis of the small intestine states that in the Rhode Island Hospital there has been one autopsy of a case of polyposis of the entire gastro-intestinal tract.

Hauser[33] in 1895 reported the case of a man of 33 who died after resection of the rectum for cancer. He had huge polypoid rectal masses and a left colon filled with polyps. There were somewhat fewer polyps in the transverse and ascending colon. In the ileum and jejunum there were small sessile polyps and in the duodenum, great numbers of polyps. In the stomach were many small polyps.

Schilling,[34] among others, mentions the dissertation of Schöttler[29] which we have been unable to obtain. This is said to be a report in detail of two instances of adenomata involving the entire gastro-intestinal tract.

Wechselman[24] reported an instance of what he impressively termed "Polyposis adenomatosa universali intestini totius," an autopsy finding in a 62-year-

old man dying of pneumonia. There was a large polyp of the stomach, another of the duodenum, and three in the jejunum, and the entire colon was thickly seeded with polyps of all sizes. Wechselman mentions, without citing it, a case previously reported which he considers questionable, and gives the list of Versé's[35] collected cases. We have reviewed the originals of the accounts quoted by Versé and the acceptable cases are included in the present report.

Funkenstein's[36] patient was a 24-year-old female who had had abdominal pain, vomiting, and bloody diarrhea for two years. She was edematous and had clubbed fingers. The red blood cell count was three million. She succumbed with a severe diarrhea. At autopsy she was found to have three pyloric polyps, six duodenal polyps, and innumerable large and small colonic polyps.

Gütig and Herzog[37] report a 16-year-old female who had been operated upon for intussusception four years before. An extensive segment of polyp-bearing small intestine had been resected. Roentgen studies showed polyps in stomach, small intestine and colon. Another intussusception occurred and at operation polyps were felt in stomach and small intestine. Death ensued. At autopsy two polyps were found in the stomach, fairly numerous large polyps in the small bowel, and two polyps in the colon.

Avidon[38] reported an 11-year-old boy with a two months' history of vomiting. Operation disclosed a polyp of the pyloric antrum which was resected. The child continued to vomit and operation disclosed a large jejunal polyp with retrograde intussusception, gangrene, and obstruction. He died after the resection, and at autopsy five gastric polyps, six small intestinal polyps, and one polyp in the colon were found.

POLYPOID ADENOMATOSIS OF SMALL AND LARGE INTESTINE

There are a number of reports of adenomatosis with this distribution of lesions. The histories combine the pain and repeated intussusception of adenomatosis of the small intestine with the diarrhea and malignant degeneration of adenomatosis of the large intestine. The condition usually is not familial. In the absence of a familial history, in patients with adenomatosis of the colon, the small intestine must be explored before a colectomy is performed. This is a therapeutically hopeless condition if the adenomata are widespread and numerous. However, resection may be feasible if the tumors involve only a few bowel segments of limited extent or if only a few large polyps are scattered about.

A Cabot[14] case report described a 36-year-old male ill with vague symptoms in the course of which he had one brief period of diarrhea and finally jaundice. Autopsy disclosed a diffuse polyposis of the intestinal tract from one millimeter beyond the pylorus to one centimeter above the internal sphincter ani. The intestine was carpeted with polyps and one, at the ampulla of Vater, had become malignant.

Mandillon and Georget[39] report a 21-year-old male whose brother died at the age of seven of intestinal obstruction and whose sister had been operated upon for intussusception due to a polyp. This patient had numerous polypoid rectal adenomata, and at laparotomy a segment of ileum two meters in length was found to bear innumerable polyps. Instead of resecting this segment the

authors removed the six largest polyps. The patient underwent four subsequent operations for intussusception of the small intestine.

In 1931 Tonnesen [40], reviewing the occurrence of intestinal polyps, stated that 73 per cent of reported cases and 82.5 per cent of his own cases of polyposis were of the rectum. For the stomach the figures were 7 and 12.5 per cent. In addition to Wechselman's cases already cited, he added one case of polyps in stomach, ileum, and colon; one in stomach, cecum, colon, and rectum; one in stomach and rectum. Tonnesen also cites the report of Aisman[41] from Russia. Aisman had two cases of polyps in ileum, colon, and rectum; one in stomach, jejunum, and ileum; one in stomach, duodenum, and colon; one in the entire intestinal tract except the jejunum.

Niemack's patient[23], a girl of twelve years, died after three years of abdominal pain and intractable bloody diarrhea. She was found to have diffuse intestinal polyposis with heaviest involvement in ileum and colon.

Versé[35] collected two instances of diffuse involvement of the ileum and two others of diffuse involvement of ileum and colon.

Schöttler[29] in addition to two cases involving the entire intestinal tract, is said to have reported one patient with polyposis of large and small intestine, two patients with polyps of the ileum, one with polyps of rectum and stomach, and one with polyps of stomach and small intestine.

Sklifasowski,[42] whose Russian report is abstracted by Port and by Mandillon and Georget, described an instance of polyposis of the entire small intestine, found at operation in 1881 in a man of 51 known to have multiple rectal polyps.

Gottesman and Perla's patient[43] died at the age of 44 after years of bloody diarrhea and had multiple polyps of large and small intestine.

The patient of Devic and Bussy[44] was a female of 36 years. She died of acute mesenteric thrombosis and was found to have multiple polyps from the proximal duodenum through the jejunum, which was practically obstructed, throughout the ileum and into the cecum and colon, which were covered with polyps down to the sigmoid where polyps became fewer.

In Farmer's[45] case there was extensive polypoid adenomatosis of the small and large intestine. There was no autopsy, and the state of the stomach is unknown except that the patient had had her first hospital admission for "gastric ulcer." She had intermittent abdominal pain and occasional vomiting but no diarrhea or melena. At her first operation two large jejunal polyps were removed. At her second operation two years later a large segment of polyp-bearing small intestine was resected. Three years after that she had a sudden collapse with massive rectal bleeding, and barium enema revealed diffuse polyposis of the rectum and colon.

Nato Campanella's case[46] is perhaps the most extreme instance of involvement of both large and small intestine in polypoid adenomatosis. An infant of five months, who had had diarrhea and occasional vomiting, developed intussusception of the jejunum and died of a massive hemmorhage. At autopsy the intussuscepted bowel appeared still viable. There was a diffuse involvement with polyps from 10 cm. beyond the pylorus to the anus.

The presence of adenomata in the stomach may complicate treatment in patients with polyps of the small intestine. Wechselman collected two such instances.

SUMMARY

Any segment of the gastro-intestinal tract and any combination of segments may be the seat of numerous adenomatous polyps.

In the colon polypoid adenomatosis is a well recognized disease entity with familial incidence. Prolonged bloody diarrhea leads to anemia and cachexia. Total colectomy is required to obviate the inevitable carcinomatous transformation of one or several of the adenomata.

In the stomach, adenomatosis causes vague symptoms. Resection of the tumor-bearing segment relieves the symptoms and prevents malignant degeneration of the polyps.

Adenomatosis of the small intestine is only occasionally familial. It is manifested by melena, anemia, and repeated intussusception. When the polyps are limited to segments of moderate length, resection is feasible.

Two cases are reported in each of which all segments of the gastro-intestinal tract were involved in polypoid adenomatosis. There are a number of descriptions of adenomatosis occurring in several segments of the bowel simultaneously and a few instances, such as those reported here, in which adenomatosis involved all segments of the gastro-intestinal tract.

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TUMOR OF THE SMALL INTESTINE*†

Miller-Abbott Tube Determines Site of Massive Hemorrhage

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RECENTLY PUBLISHED LITERATURE contains many reports of cases of massive hemorrhage from the gastrointestinal tract. An article by Baker and Halley includes an excellent review of the recent outstanding literature dealing with benign tumors of the small intestine and covers the subject well. Such a review here would be repetition.

Numerically, tumors of the small intestine are about equally divided between the benign and the malignant type. By far the commonest malignant tumor is the adenocarcinoma. In an article read recently before the Georgia Medical Society, Good stated that 26, or approximately 42 per cent, of a series of 61 tumors of the small intestine seen at the Mayo Clinic were adenocarcinomas, and 10, or about 16 per cent, were leiomyomas. While leiomyomas constitute only a small percentage of the tumors of the small intestine, there is frequently doubt as to whether they should be considered benign or malignant. It is certain that many of them eventually become malignant.

Tumors of the small bowel, whether benign or malignant, occur most frequently in the proximal portion. Symptoms are variable and by no means dependable, but the commonest one is bleeding, which is estimated to occur in about 35 per cent of cases.

The case reported here is one of massive intestinal hemorrhage from a tumor of the small bowel. Histologically, this tumor appeared to be benign, but it was classified by the Army Institute of Pathology as a leiomyosarcoma. This case illustrates many of the common symptoms of this condition as well as some of the diagnostic difficulties encountered.

REPORT OF CASE

M. E. G., Sr., a white man aged 63, was admitted to the Fort McPherson Station Hospital on March 5, 1947 in a state bordering on shock. Approximately two hours previously, he had fainted without warning in a downtown hotel lobby and when taken to his room, had had two copious stools of dark red blood. When he was admitted to the emergency room of the hospital, he complained of cramps in the lower portion of the abdomen and extreme weakness. He estimated that he had passed approximately 1 quart of dark blood per rectum before admission.

Approximately 10 years prior to this time, the patient had experienced a similar episode, following which a complete roentgen examination of the gastro-intestinal tract together with appropriate hematologic studies had been made, with negative results except for a slight filling defect of the duodenum. Exploratory laparotomy at that time had revealed an entirely normal stomach and duodenum. No reason could be found for the slight roentgen evidence of irregularity in the duodenum. The small intestine had

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appeared entirely normal. With the exception of vague indigestion and irregular bowel habits, the patient had lived normally until approximately four months prior to admission, at which time he had had another massive intestinal hemorrhage. Roentgen studies had demonstrated the presence of a small diaphragmatic hernia. It was suspected that the hemorrhage had resulted either from an ulcer in the lower portion of the esophagus or the upper part of the stomach, or from esophageal varices. The bleeding had stopped completely, and no further treatment was sought.

Physical examination revealed a well developed and nourished white man, lying quietly in bed in no acute pain. He was extremely pale, almost matching in color the sheets on the bed. The pulse was weak but regular, with a rate of 100; the temperature was 97.6 F. Aside from slight generalized abdominal tenderness, the physical examination gave essentially negative results. The red blood cell count was 4.1 million with hemoglobin 70 per cent (12 Gm. Sahli); the hematocrit reading was 26 cc. per hundred cubic centimeters of blood; the total protein content was 5.75 Gm., the albumin 3.10 Gm. and the globulin 2.65 Gm. per hundred cubic centimeters of blood; and the albumin-globulin ratio was 1.17 to 1.

The patient was given plasma and heavily sedated. The following morning, he was given 500 cc. of whole blood slowly, with no further evidence of hemorrhage. At this point, with 2,000 cc. of matched blood available, a Miller-Abbott tube was passed for diagnostic purposes. The bleeding point was established approximately 5 feet beyond the stomach. He was then given a liquid diet high in protein and carbohydrates, and was transfused at intervals. On March 9, the hematocrit reading was 32 cc., and the red blood cell count was 3.5 million. It was decided that this would be an ideal time for exploration as his general condition seemed excellent.

At operation, the incision was made in the right upper quadrant of the abdomen through the scar resulting from the previous laparotomy, and the peritoneum was opened with difficulty because of underlying omental adhesions. These adhesions were dissected free, and the peritoneal cavity was entered. Careful examination of the liver revealed no nodules and no evidence of metastasis. The gallbladder emptied normally. Because of rather dense adhesions, the stomach and duodenum were not examined. Starting at the ligament of Treitz, the small intestine was carefully examined throughout its entire length. Approximately 3 feet from the duodenum, a small intussusception was encountered, which reduced spontaneously as it was examined. No cause could be found for the intussusception, and at the close of the operation its exact location could not be determined by examining the bowel. Approximately 4 feet from the duodenum, a large intussusception was demonstrated. The cause for this was a small tumor (Fig. 1) on the antimesenteric side of the intestine. There was great increase in vascularity in the mesentery at this level. One or two small buckshot-sized nodes were palpable near the intestine in the mesentery, but no distant nodes could be palpated. The bowel was resected approximately 4 inches on either side of the tumor, and an end to end anastomosis was performed. Routine closure of the abdominal wall was carried out, and the patient's immediate postoperative condition was satisfactory.

On the day following the operation, the total protein content of the blood was 5.68 Gm., albumin 3.54 Gm. and globulin 2.14 Gm.; the albumin-globulin ratio was 1.65 to 1. The general condition of the patient seemed excellent. On the second postoperative day, the blood values were total protein content 5.11 Gm., albumin 3.75 Gm. and globulin 1.36 Gm.; the albumin-globulin ratio was 2.7 to 1. At this time the red blood cell count was 3.55 million, the hemoglobin 58 per cent (10 Gm. Sahli), and the hematocrit reading 31 cc.

From this point the patient made an uneventful recovery. Sutures were removed on the eighth postoperative day, at which time the wound was well healed. The red blood cell count was at that time 3.6 million with hemoglobin 73.5 per cent (12.5 Gm. Sahli). He was allowed out of bed on the fourth postoperative day and by the eleventh

day was able to be up most of the time. He was discharged from the hospital on this date.

The pathologic report from the Army Institute of Pathology follows: "The tumor nodule, which is well circumscribed, lies in the wall of the jejunum. It interrupts the muscular layer laterally, closely underlies and elevates the epithelium on the mucosal aspect, and extends to the serosa by way of a nipple-like extension. Its structure is compact, consisting of fusiform-shaped cells arranged in interlacing strands and bundles.

FIG. 1.—This photograph shows the tumor protruding into the jejunum.

The nuclei, depending upon the plane of section, are round to rod-shaped. They are rather pale with finely granular diffusely scattered chromatin and a single moderately conspicuous nucleolus. There is mild variation in the size and shape and staining qualities of the nuclei. Mitotic figures are not seen. The appearance and staining properties of the cells indicate an origin from smooth muscle. Vascularity is moderate; the vessels are thin-walled, consisting in many instances of only an endothelial layer which appears to be directly opposed to the tumor cells. In recognition of the treacherous course of smooth

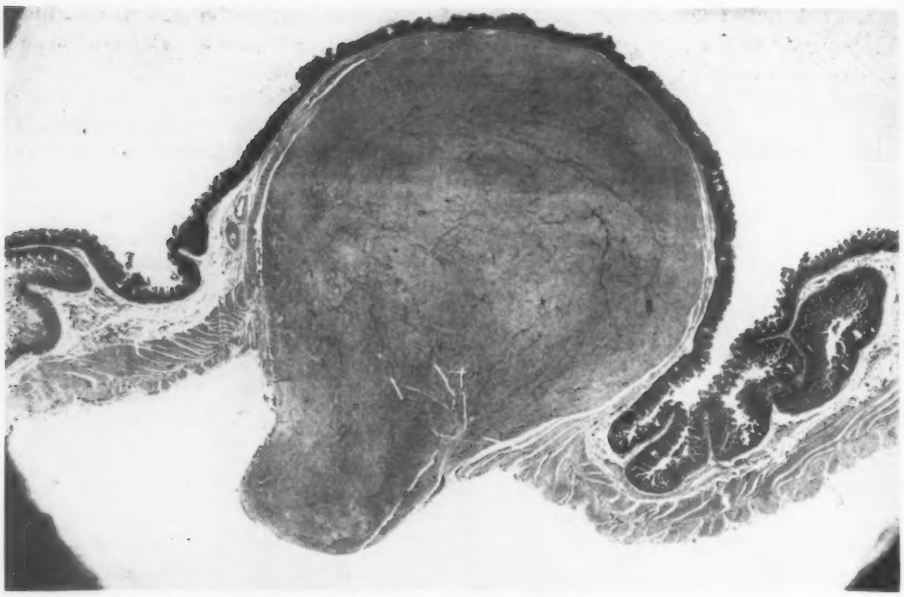

FIG. 2.—Photomicrograph showing a cross section of the tumor (magnified 6 times).

muscle tumors of the intestine, the lesion in this case is being coded as a leiomyosarcoma despite its relatively innocent histologic appearance" (see Fig. 2).

DISCUSSION

This case is being reported largely for a discussion of the diagnostic procedure used. It is recognized that this procedure has great potential dangers, and, except for the fact that the patient had had two previous severe hemorrhages followed by every conventional diagnostic test including exploratory laparotomy, it would have been considered too dangerous to use. With 2,000 cc. of blood matched with that of the patient ready for immediate use, a Miller-Abbott tube was passed into the stomach and the contents aspirated and tested for blood. It was then passed under fluoroscopic vision through the duodenum with samples being taken in the second and third portions of the duodenum. The tube was then advanced approximately 6 inches at one hour intervals, and a sample of the intestinal content was withdrawn each time. When the tube had been passed approximately 5 feet beyond the end of the stomach, dark blood was withdrawn for the first time. A roentgenogram was made to establish the location of the tube, and the tube was thereafter immediately withdrawn.

The Miller-Abbott tube gave an accurate picture of the location of the source of this patient's bleeding. It made possible exploratory laparotomy with a fairly definite aim in view. Exploration revealed the tumor at approximately four feet from the ligament of Treitz, or about where it was expected the lesion would be found. The tumor was evident and would have been easily discovered upon exploration, but since one exploration almost ten years previously had

failed to demonstrate the site of hemorrhage, it was feared that the same difficulty would be encountered again. It is by no means certain that the first hemorrhage which the patient experienced was due to the same lesion as were the last two hemorrhages.

This procedure is not recommended as a routine diagnostic aid. It is thought, however, that in rare instances when plenty of blood is available and immediate surgery can be instituted, it may be a helpful diagnostic aid.

SUMMARY

Tumors of the small intestine are discussed briefly.

A case is reported in which the pathologic diagnosis was leiomyosarcoma of the jejunum.

In this case massive hemorrhage was localized by the passage of a Miller-Abbott tube.

Despite its potential dangers, this procedure may occasionally be a valuable diagnostic aid in selected cases.

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RECURRENT PRIMARY THROMBOCYTOPENIC PURPURA WITH ACCESSORY SPLEENS*

Review of the Literature

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WERLHOF in 1731, laid the foundation for our present concept of the disease which bears his name, and which also is described as "purpura hemorrhagica." However, in the eighteenth century, the spleen was unsuspected of being associated with thrombocytopenic purpura. In 1916, Kaznelson,[2] while still a medical student, favored the theory that hypersplenism was responsible for lowered platelet counts. This resulted from an observation which he made, namely, that in three of four cases of thrombocytopenic purpura, he found a splenomegaly. At his insistence, he persuaded Shloffer of Prague to do a splenectomy on a patient suffering from chronic thrombocytopenic purpura; this resulted in a dramatic response. In 1921, Finkelstein[3] was probably the first to call attention to the fact that accessory spleens might be responsible for the recurrence of symptoms in postsplenectomy essential thrombocytopenia, and in 1928, Morrison, Lederer and Fradkin[4] reported two cases of accessory spleens associated with this condition. The role played by unremoved accessory spleens following splenectomy for primary thrombocytopenic purpura has been stressed by Curtis and White,[5] Vaughan,[6, 7] Robertson,[8] Maingot,[9] Curtis and Movitz,[10, 11] and Watson and Moir.[12]

Despite the fact that such significance has been placed upon unnoticed splenicules, few cases are reported. Watson and Moir[12] record recurrent purpuric manifestations in a case following therapeutic splenectomy in which a 2.5 cm. diameter accessory spleen was found at necropsy. A similar case appears in the article of Curtis and Movitz.[11] These latter two authors have established the importance of accessory spleens in showing that in 174 consecutive cases of splenectomy, and in four abdominal explorations, they found 131 accessory spleens in 56 patients, an incidence of 32 per cent. The number of accessory spleens varied from one to ten.

Recurrence of primary thrombocytopenic purpura is reported by Giffin and Holloway[13] as 14 per cent, and Vaughan[7] as 17 per cent. What percentage of such recurrences results from accessory spleens is unreported, but it is suggested by Watson and Moir,[12] that the incidence of the recurrences closely resembles that of accessory splenic tissue reported by pathologists. Adami and Nichols[14] report 11 per cent in their necropsies; the incidence at Cook County Hospital is 10 per cent; Emmet and Dreyfuss[15] record 10 per cent and Morrison et al[4] report 35 per cent after adoption of a systematic search. Increased incidence of accessory tissue in primary splenic disease is reported

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by Maingot[16] (44.4 per cent), Curtis and White[5] (20 per cent), McLaughlin[17] (24 per cent), and Curtis and Movitz[11] (31.4 per cent).

Splenic "seeding" should be considered during the removal of the spleen for such diseases as primary thrombocytopenic purpura and congenital hemolytic icterus, especially when recurrence follows. Such accidental "seeding" is suggested by Curtis and Movitz.[11] McLaughlin[17] has reported a case of recurrent congenital hemolytic icterus in a splenectomized patient, in whom generalized so-called abdominal "hemolymph" glands were found enlarged at necropsy; it was thought that these were splenic type tissue. The successful transplantation of such tissue into subcutaneous and muscle layers by Putschar[18] and Perla,[19] and the observation by several writers[20-29] of multiple intra-abdominal splenic tissue islets following trauma to the spleen, suggests the possibility of relapse by gradual assumption of splenic functions by these new growths. No instance, however, is reported in which such nodules following surgery for rupture of a normal spleen have resulted in primary splenic disease.

Buchbinder and Lipkoff[29] have termed the "seeding" of multiple splenic transplants through the abdominal cavity following splenic trauma as "splenosis," and this condition technically should be differentiated from the presence of true accessory splenic tissue. It is probable that the 400 accessory spleens reported in 1896 by Albrecht[20] and the case he cites by Orth were of this category.

While "splenosis" as described above follows no general plan, there are certain generalities to be noted concerning the locations of true accessory spleens. Since minuteness in no way eliminates the tissue as a cause of future recurrence, a definite plan of search should be followed to remove these offenders. Schilling[21] lists the possible sites in this order of frequency: (1) splenic hilus, (2) gastrosplenic omentum, (3) great omentum, (4) edge of the omentum, (5) splenocolic ligament, (6) pleurocolic ligament, (7) peritoneum along the splenic vessels, and (8) pancreas. Curtis and Movitz[10, 11] list: (1) the hilus of the spleen, (2) the pedicle of the spleen, (3) the retroperitoneal region around the tail of the pancreas, (4) the omentum, especially at the greater curvature of the stomach, (5) splenocolic ligament, (6) the mesentery of both small and large bowel, and (7) the left adnexa in females. The latter authors surprisingly found that 85 per cent of patients with accessory spleens had them in a single location, and that in no instance were more than two locations found. In addition, where such was the case, one of the double sites was always hilar. Even in unusual cases, such as Olken's,[30] a second hilar accessory was found in addition to a left scrotal splenicule.

EMBRYOLOGY

Splenic anlagen first appear in the 8 mm. embryo,[31] on the left side of the dorsal mesogastrium, as an accumulation of mesenchymal cells, just beneath the surface (peritoneal) epithelium. These appear as several small "hillocks" whose subsequent fusion forms a single organ. The survival of one of these may result in a lobulated or accessory spleen. Whether this abnormality occurs

cephalad, caudad or ventrad to the main mass, and whether it arises early or late in embryonic life determines roughly the location of the splenicule.

Curtis and Movitz[11] have given an excellent review of the underlying embryologic principles and consider five phases of splenic development sufficient to explain all accessory spleens. They are the following: (1) the manner of formation of the major spleen with its notches and lobulations by fusion of the separated splenic masses; (2) the formation of accessories by failure of fusion of the separate anlagen; (3) the formation and development of the subjacent dorsal mesogastrium into the various ligaments and bursae carrying along the accessory spleens to their various distant future locations; (4) the development of the splenic artery and its branches providing a similar blood supply to the splenic lobules and the accessories, with the accessory merely representing a greater degree of "fusion failure" than the lobule; (5) the embryonic contiguity of splenic anlagen to the genital ridge (on medial side of the mesonephros) permitting an accessory spleen to become attached to the left gonad.

Although the spleen is part of the blood system of the body, Keith[32] considers its development with organs of digestion since he thinks it must originally have been part of the alimentary system. Its origin is connected with the stomach, and its blood like the alimentary tract enters the portal circulation. The spleen grows from the left surface of the dorsal mesogastrium above the cardiac end of the stomach. It appears at the beginning of the sixth week as a localized growth of mesoderm. In the third month, the dorsal splenic surface is nodular and deeply fissured, and at the middle of fetal life these fissures begin to disappear but only persist on the anterior (gastric) border.

PATHOLOGIC PHYSIOLOGY

C. A. Doan[33] has done much to clarify the modern concept of the physiology of the spleen from an organ of complete mystery to one of understandable functions. Although much information concerning the spleen is controversial, certain facts seem fairly well established. This organ seems to have the following three structures: (1) a reticulo-endothelial system; (2) a vascular system; (3) a lymphoid system. The smooth muscle in the capsule and trabeculae together with the vascular system serve as the structural basis for the blood reservoir function of the spleen. The reticulo-endothelial system is made up of "specific endothelia," and a reticulum endowed with special phagocytic powers.

The normal spleen is concerned with blood cell destruction, formation and sequestration. A delicate splenic equilibrium results which may be upset by either congenital or acquired causes, resulting in diminution or accentuation of these physiologic processes. By means of supravital studies on splenic parenchyma, it has been shown that the spleen may become hyperactive with a resulting increase in number and phagocytic power of the macrophage. This has been referred to as hypersplenism. If this overactivity focuses on the red blood cells, congenital hemolytic icterus results; if it focuses on the thrombo-

cytes, then essential thrombocytopenic purpura results; and if the granulocytes are affected by the destructive process, a condition designated as primary splenic neutropenia results.[34]

When such a spleen becomes hyperactive, the bone marrow tries to compensate for the destruction and loss of blood elements. However, the spleen usually gains the upper hand and the involved blood cells are kept at a pathologic low level. Should an overactive spleen fail to discriminate between the elements which pass through it, red cells, granulocytes and platelets all may be destroyed simultaneously, resulting in a condition called pansplenic hematocytopenia. In such patients, a marked compensatory hyperplasia of the bone marrow results.

CASE REPORT

J. H. (46-58183), a 22-year-old white married female, entered Cook County Hospital November 25, 1946, complaining of an aching pain in the "right side" for 4 days, which was accompanied by vomiting and constipation.

History. History revealed that the patient, in her youth, suffered severe epistaxis once every two months, and also had marked gingival bleeding. After menarch at 14 years, she experienced prolonged menstrual periods which always lasted from one to two weeks with onset at 30-day intervals. These were described as not excessive but merely prolonged.

In April 1943, a slight injury resulted in a large bruise over the anterior forearm and arm. She consulted her family doctor who immediately had her hospitalized for observation. She recalls the diagnosis as "purpura" and states that she received "shots" in the deltoid area; however, she stopped these voluntarily.

In August 1943, following severe vaginal bleeding, the patient consulted a gynecologist and was immediately hospitalized. She received 6 transfusions, and a splenectomy was performed. She remained in the hospital for about 2 weeks, her vaginal bleeding stopped, and the small red spots which were present on her legs gradually disappeared. Postoperative platelet counts unfortunately were not done.

Thirty days after the preceding hemorrhage, another severe vaginal hemorrhage occurred and following its cessation, in approximately 10 days, the patient received radium therapy via a vaginal pack. Although her ecchymoses and gingival bleeding persisted and the small red spots continued to appear, she had no vaginal bleeding until May 1945, when she had a scant three-day flow. These facts should have made one suspicious of the presence of accessory splenic tissues.

In May 1946, the patient consulted her local doctor because of severe pain in the left side and back and was told she might be pregnant. In the latter part of April, the vaginal bleeding recurred and the fourth day after its onset, May 2, 1946, she entered the Cook County Hospital as a threatened abortion case. She was treated for shock and severe anemia by multiple transfusions of whole blood. A blood count done on May 3, 1946, revealed RBC 1.06, WBC 33,700, Platelets 252,290 and Reticulocytes 4.9. A marrow smear was reported as not unusual, and it was the impression of the hematologist that local genital pathology was the cause of the prolonged hemorrhage. On May 11, 1946, a currettement was done with negative gross and microscopic findings, and on May 22, 1946, she was operated upon and the left tube and ovary were removed. Diagnosis: hematosalpinx and hemorrhage into an ovarian cyst. No further platelet counts were done and the patient left the hospital on the twenty-ninth day.

At the present admission, she complained of pain just above the right iliac crest which was present for 4 days, and was dull and aching in character. She was awakened during this period each morning at 4:00 A. M., by a pronounced desire to defecate but was unable to have a bowel movement. Nausea and vomiting of clear fluid relieved the

urge to defecate without alleviating the pain. This sequence was repeated once each afternoon during the present illness with no relation to hour, food intake or activity. Voluntary dietary restrictions were imposed. On the day of admission, she was again awakened with the desire to defecate, but had relief following a small clear liquid emesis which this time contained specks of blood. Upon admission to the Cook County Hospital the

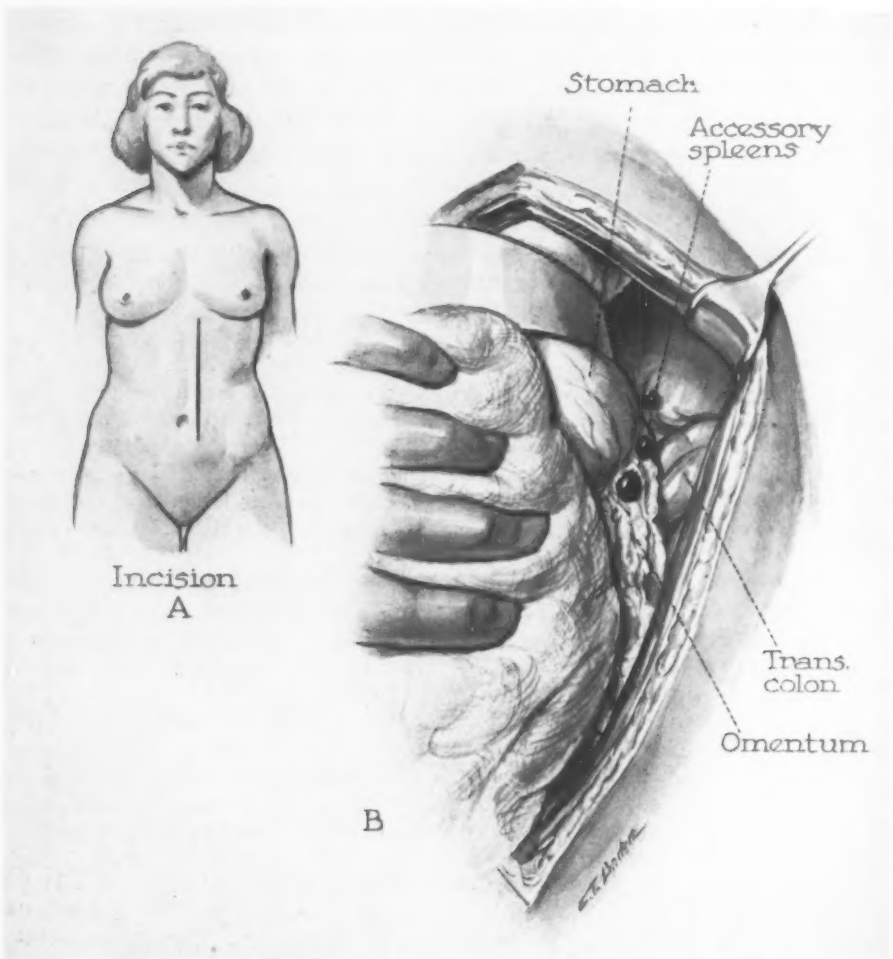

FIG. 1. (A).—Longitudinal left transrectus incision gave adequate exposure.
(B).—The three accessory spleens as seen at surgery.

patient gave no history of drug or medication ingestion nor of recent illnesses. The family history was essentially negative and venereal disease was denied.

Physical Examination. Physical examination revealed a pale, thin white female who did not appear acutely ill. Blood pressure 110/80, pulse 90, respirations 18, and the rectal temperature was 99.8. Several large ecchymotic patches were found over the body unassociated with trauma. The abdomen was soft, not tender, and no masses could be palpated. Bowel sounds were somewhat hypo-active. Left subcostal and Pfannensteil scars were well healed. The pelvic examination was non-contributory except for a very firm, regular cervix and vault, and adnexal adhesive distortion. A Rumpel-Leeds test was negative.

FIG. 2.—The largest of the three accessory spleens located in the omentum near the previously ligated splenic pedicle.

Treatment. The patient was placed on a high-protein, high-carbohydrate diet with supplemental vitamin and iron therapy. On November 27, 1946, the second day of hospitalization, a platelet count was 77,280. It was at this time that the possibility of accessory splenic tissue presented itself. On November 30, 1946, platelets numbered 6,850 and a normal cell count and differential were recorded. Vigorous intravenous therapy was started, giving at least 500 cc. of blood daily in addition to other parenteral fluids. An elimination diet was begun, all medication stopped, and the patient held in readiness for emergency exploratory laparotomy in search of accessory splenic tissue if significant increase in peripheral platelets did not occur. A sternal puncture at this time revealed a marrow with slightly increased granulopoieses and a right shift, but with megakaryocytes and eosinophiles in normal numbers; findings were compatible with the clinical diagnosis of recurrent thrombocytopenic purpura. Chest plate and barium studies revealed no pathology. Preoperative bleeding time was 8 minutes 5 seconds; coagulation time was 4 minutes 10 seconds. Elimination diet was discontinued since the thrombopenia was apparently not on an allergic basis; on December 4, 1946, the Rumpel-Leede test was positive.

On December 5, 1946, under pontacaine spinal anesthesia, an exploratory operation was performed, by Dr. P. T., through a longitudinal left transrectus incision. It was noted during the entire course of the operation that there was a marked tendency to bleed. Three accessory spleens were found (Fig. 1). The largest approximately the size of a cherry (Fig. 2), the second about the size of a pea and the third that of a pinhead. The first two were close to each other and were located in the omentum near the previously ligated splenic pedicle. The smallest spleen was found along the upper border of the tail of the pancreas. Macroscopically it was difficult to differentiate the latter from a tiny lymph node. Microscopic sections on all three specimens definitely established each as being an accessory spleen with the following description: the section revealed dilated sinusoids with a slightly hemorrhagic pulp and marked proliferation of mononuclear cells and a few polymorphnuclear leukocytes. The malpighian corpuscles were large. The pathologist concluded that these findings were in keeping with a diagnosis of thrombocytopenic purpura.

Following the removal of these masses, there was no dramatic cessation of bleeding; in fact, gingival hemorrhage of a moderate sort continued for two postoperative days despite whole blood transfusions. On the second postoperative day her clotting time was 9 minutes 17 seconds and bleeding time was 6 minutes. On the third postoperative day, all gum bleeding stopped, even though menstruation which began on December 2, 1946, continued. On the fifth postoperative day, December 10, 1946, the bleeding time was normal, platelets numbered 95,200 and the patient was up and about; menstruation ceased. Clinical improvement paralleled subsequent platelet increases and the patient left the hospital on December 21, 1946, with a platelet count of 750,000 to be followed as an out-patient.

The patient did remarkably well until January 8, 1947, when she again noted petechial hemorrhages and bleeding from the mouth. This increased in severity. She was readmitted. Repeated platelet counts varied between 0 and 14,000. She was reexplored on another surgical service January 14, 1947, and no additional splenic tissues could be found. However, on January 22, 1947, her platelet count had risen to 92,360. The patient gradually improved, her bleeding stopped and upon discharge from the hospital was clinically improved. She will be followed in the out-patient department. Whether or not tissue damage following surgery may stimulate platelet formation or not is theoretical. It seems more logical to conclude that splenic "seeding" might have occurred, or that ectopic splenic tissue still may exist in some very remote anatomical recess.

Many other methods of therapy have been advocated, especially in chronic cases, such as snake venom, cevitamic acid, roentgen-ray, viosterol, parathyroid extract and rutin, but these usually fail to produce the desired results.

The treatment for purpura hemorrhagica is splenectomy. This is an emergency procedure in the acute cases, and may be elective if the condition is chronic. The possibility of accessory spleens must be kept in mind, a search made for these, and if found they must be removed. Repeated transfusions with freshly removed matched blood (not bank blood) supply effective platelets. Hemorrhagic manifestations usually disappear while the patient is still on the operating table, and the platelet count rises immediately.

SUMMARY

1. A case of recurrent primary thrombocytopenic purpura associated with the removal of three accessory spleens is reported.

2. The literature is reviewed.

3. The importance of searching for accessory splenic tissue at the time of operation is emphasized.

4. The pathologic physiology of the spleen is reviewed.

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STREPTOMYCIN IN SURGICAL INFECTIONS

Part VI. Lung Abscess and Empyema*

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THE LITERATURE ON STREPTOMYCIN in bronchial and pulmonary infections is not extensive. Good results have been reported to follow its use in infections caused by Klebsiella pneumoniæ (Friedlander's bacillus) and Hemophilus influenzae (Pfeiffer's bacillus) as well as in tularemic and acute tuberculous pneumonias.[1, 2, 3] These results have been confirmed in U. S. Army hospitals.[4] Bronchitis and bronchiectasis have been consistently benefited only when streptomycin has been given in combination with penicillin. In asthma associated with chronic respiratory infection a limited therapeutic trial of streptomycin has not been encouraging.[4]

Reports on the use of streptomycin in pleuropulmonary infections are even more limited. The Committee on Chemotherapeutics and Other Agents of the National Research Council reported its employment in five cases of nontuberculous empyema but supplied no details except that three patients were unimproved.[1] The Council also reported improvement in only one of eight patients with tuberculous empyema treated by this method and concluded, on the basis of these observations, that the method was not useful. Kane and Foley[3] thought that the combined penicillin and streptomycin aerosol therapy of pulmonary abscess had been useful in a single case caused by Hemophilus influenzae. Fisher and Shaw[5] attributed to combined intramuscular and intrapleural streptomycin the rapid cure of a 10-year-old girl with empyema caused by Hemophilus influenzae. The only other report in the literature, from Buenos Aires, concerns two cases of empyema treated by intrapleural injections of streptomycin; the immediate improvement which occurred was not sustained when therapy had to be discontinued because the supply of the drug was inadequate.[6]

This communication, the sixth in a series dealing with the treatment of surgical infections by streptomycin in U. S. Army hospitals, is concerned with the results of this type of therapy in lung abscess and in empyema of both tuberculous and nontuberculous origin. The material, which was supplied to the Office of the Surgeon General by participating Army hospitals, consists of three cases of lung abscess, five cases of non-tuberculous empyema and nine cases of tuberculous empyema. Critical analysis of the case reports which make up this small series has permitted certain conclusions as to the efficacy of streptomycin therapy in these conditions.

LUNG ABSCESS

Case 1.—A 39-year-old man, following a "head cold" of five weeks' duration, developed a productive cough, fever, sweats, and shortness of breath. He entered the hospital

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in the sixth week of his illness, during an acute exacerbation of these symptoms. Physical examination and roentgenographic studies were consistent with a diagnosis of abscess of the right upper lobe. Penicillin given intramuscularly in doses of 40,000 units every three hours and general supportive measures produced no results at the end of 6 days. On the following day thoracotomy was performed, the findings including a cavity approximately 10 x 5 x 10 cm. and a bronchopleural fistula. Open drainage was instituted and a pack was applied. Culture of the pus yielded mixed organisms, including pneumococci.

After operation penicillin was continued by the preoperative routine and was supplemented by streptomycin given in 0.6 Gm. doses intramuscularly every 4 hours. In addition, a streptomycin solution containing 2 mg. of the drug per ml. was instilled 3 times daily onto the pack in the abscess cavity; the solution was nonirritating and it seemed to reduce to a considerable degree both the odor and the amount of the drainage. The patient demonstrated progressive clinical improvement and after the fifth day had no temperature elevations. Serial roentgenograms revealed subsidence of the pneumonitis surrounding the lung abscess and a progressive decrease in the size of the cavity.

Case 2.—A 29-year-old man entered the hospital with a far-advanced bronchiectasis involving all the lobes of the right lung, an abscess of the right lower lobe, a severe cough productive of 75 to 150 ml. of foul sputum daily, and a 60-pound weight loss. His illness had been of two years' duration.

Inhalations of penicillin, repeated bronchoscopic aspirations, postural drainage and supportive therapy were without effect. Repeated examination of the sputum revealed numerous gram-negative organisms, but no acid-fast bacilli. Parenteral streptomycin therapy was therefore begun, with the hope of bringing about healing of the lung abscess, and 290 Gm. were given over a 76-day period. The sputum expectorated did not decrease in amount, and there was continued destruction of the lung tissue around the abscess. Death occurred three days after streptomycin had been discontinued.

Case 3.—A 25-year-old soldier developed extensive cavitation of the right lower lobe subsequent to pneumonitis. During 8 days of treatment with penicillin the temperature averaged 102° F. Cultures of the sputum revealed a variety of streptomycin-sensitive gram-negative bacilli and gram-positive cocci. No immediate response followed the parenteral administration of streptomycin in dosages of 1 Gm. daily, and on the fifth day of treatment roentgenograms revealed no change in the extent of cavitation. The following day, however, the patient coughed up a large amount of sanguinopurulent material and the temperature promptly returned to normal.

COMMENT

The role of streptomycin is difficult to evaluate in the first of these three cases, since sensitivity tests were not carried out on the bacterial cultures and penicillin was given before operation as well as in combination with streptomycin after operation. The only positive results were noted after local instillations of streptomycin, in the form of a decrease in the odor and amount of drainage. It is possible that this patient might have responded just as well if streptomycin had been omitted and treatment had been limited to surgery and penicillin. In the second case the pathologic changes, which were far advanced and of a progressive character, were not influenced by a 76-day course of streptomycin. In the third case, in which a relatively early lung abscess was caused by streptomycin-sensitive organisms, the administration of the antibiotic was possibly helpful in reversing the progress of the infection. The evacuation of pus and the subsequent alteration of the course of the disease occurred after only six days of streptomycin therapy, it is true, but it is well known that edema of the main bronchi and immediate branches may

respond favorably after only a few days of specific chemotherapy. The dosage in this case, 1 Gm. per day, is lower than the usual dosage, but was apparently adequate in this instance.

NONTUBERCULOUS EMPYEMA

Case 4.—A 26-year-old man, following a nontraumatic perforation of the sigmoid colon, successively developed peritonitis, a right-sided subdiaphragmatic abscess, and a severe right-sided empyema. When the subdiaphragmatic abscess was drained a probable intrahepatic abscess was demonstrated. Shortly afterward a massive collapse of the right lung occurred. It partially re-expanded, but the patient's condition became critical.

Culture of pus from the chest, 150 ml. of which was removed by thoracentesis, revealed Escherichia coli as the predominating organism. Streptomycin therapy was therefore begun, in the amount of 2.4 Gm. daily by the intramuscular route and 2.0 Gm. daily by the intrapleural route, after aspiration. The result was prompt and gratifying. The temperature, pulse and respiration fell to normal levels, there was no further weight loss, and the patient's appetite improved. By the end of 26 days of treatment his condition was sufficiently stabilized for right thoracotomy to be done, with drainage of the residual empyema. Streptomycin was continued by the intramuscular route for 8 days after operation; at the end of this time the temperature was normal. The patient remained permanently afebrile and the empyema cavity ultimately was obliterated.

Case 5.—This patient, a 24-year-old man, required thoracotomy with open drainage for a right-sided empyema following peritonitis of appendiceal origin. Cultures of the pus from the chest grew mixed aerobic and anaerobic gram-negative rods and gram-positive cocci, all of which were susceptible to streptomycin. After operation penicillin in dosages usually adequate (320,000 units per day) failed to produce the usual results, and on the fourth postoperative day streptomycin, in dosages of 3 Gm. daily, was added to the therapeutic regimen. Progressive improvement occurred and was sustained when therapy was discontinued at the end of 13 days. At the end of 2 weeks the temperature was normal and the empyema cavity, which had become greatly reduced in size, was continuing to close rapidly.

Case 6.—A 21-year-old soldier, who sustained a penetrating pistol shot wound of the left chest, with hemopneumothorax, had been treated overseas with intercostal tube drainage, supportive therapy, and 30,000 units of penicillin intramuscularly every 3 hours. In the Zone of Interior cultures from the lesion revealed staphylococci and Klebsiella pneumoniae, both of which were sensitive to streptomycin. Roentgenograms showed two distinct pockets of fluid.

Penicillin was administered in adequate dosages for 2 weeks, without demonstrable clinical response. Streptomycin was then added to the regimen in the amount of 1.2 Gm. daily by the intramuscular route. In addition, daily thoracenteses were carried out in the pockets not drained by the intercostal tube and were followed by instillations of 200 ml. of a solution containing 0.5 Gm. of streptomycin and 40,000 units of penicillin. The response was dramatic clinically as well as bacteriologically. On the second day of treatment the aspirate grew only *Staphylococcus aureus* and on the fourth day it was clear and sterile. There was no temperature elevation after the fourth day. Intramuscular injections of both antibiotics were continued for 7 days and intrapleural injections for 10 days. The fluid in the chest became progressively clearer and scantier, and at the end of 2 months was completely absorbed.

Case 7.—An 18-year-old soldier with unresolved pneumonia of the left lower lobe on a bronchiectatic basis developed an acute sacculated empyema of the left pleural cavity with a pronounced constitutional reaction. Aspiration yielded thick greenish-yellow pus from which streptomycin-sensitive *Hemophilus influenzae* and anaerobic nonhemolytic streptococci were grown.

Penicillin and sulfadiazine were both ineffective. Streptomycin (0.5 Gm. by the intramuscular route) was then given every four hours for ten days. At the same time, an

attempt was made daily or every second day to empty the various loculated empyema cavities and to replace the aspirate with 0.25 Gm. of streptomycin in solution. For 3 days after this treatment was begun the temperature was lower and the patient improved appreciably. Then drainage of the pockets by aspiration became increasingly difficult and the temperature returned to its formerly high peaks. Eventually the cavity was completely obliterated by thoracotomy with open drainage, under cover of parenteral penicillin and streptomycin. Three months later a plastic operation on the chest wall was carried out, and the soldier was in good condition when he was subsequently separated from Service.

Case 8.—A 38-year-old man, first seen in June, 1947, had a persistent empyema cavity as the result of a shell fragment wound in 1944. A thoracotomy and several thoracoplasties had been ineffective. In July, 1946, decortication of the empyema space was followed by a breakdown of the wound, which eventuated in a saucerized cavity and the exposure of a large area of visceral pleura. Hemolytic *Staphylococcus aureus* infection was persistent and the course was septic. An attempt at a split thickness skin graft was not successful.

In July, 1947, culture of material from the empyema cavity again yielded hemolytic *Staphylococcus aureus*, which was now resistant to penicillin. The organism was, however, sensitive to streptomycin, which was given in dosages of 2 Gm. daily by the intramuscular route. The temperature almost immediately returned to normal and the amount of drainage decreased. The cavity was then packed with gauze saturated with 1 Gm. of streptomycin in physiologic salt solution, and several negative cultures were secured over a 10-day period. It was now possible to carry out decortication of the visceral pleura, a plastic operation on the thoracic muscles, and closure of the chest wall. The wound healed promptly and firmly and the patient was in good health when he left the hospital after operation.

COMMENT

In this group the two patients with empyema complicating peritonitis of fecal origin undoubtedly derived a beneficial cumulative effect from streptomycin-penicillin therapy employed as an adjuvant to adequate surgical drainage. In Case 4, in fact, streptomycin therapy was probably life-saving. In Case 6, in which the empyema originated in a combat injury, the results were equally good; the elimination of streptomycin-sensitive organisms and then of penicillin-sensitive staphylococci might not have been achieved had either antibiotic been employed singly. Case 7 emphasizes the difficulties and unwisdom of attempting to manage a loculated empyema cavity without adequate surgical drainage. Streptomycin was not effective, and could not have been expected to be effective, until thoracotomy had been carried out. Case 8 illustrates radical curative surgery which was made possible by the judicious local application of streptomycin. The systemic use of the antibiotic would not have been effective alone in this case since bacteriostatic concentrations by way of the blood stream are not achieved in fibrotic, poorly vascularized tissues. In this case the indications for streptomycin therapy were clear-cut, as the staphylococci had lost their susceptibility to penicillin.

TUBERCULOUS EMPYEMA

Streptomycin was tested in Army hospitals in nine cases of tuberculous empyema, six of which were treated by surgical measures also. One of the patients treated only by medical measures had advanced chronic pulmonary tuberculosis of all lobes of the left lung, a right bronchopleural fistula, and a mixed tuberculous empyema for which open thoracotomy had been done. The

daily dosage of streptomycin consisted of three Gm. by the intramuscular route, with an additional one to two Gm. directed through the thoracotomy wound by means of the aerosol spray. The first response was encouraging. Over a period of two months drainage decreased, healthy granulations developed around the wound, and the fistula closed. The fistulous tract, however, reopened within the month, in spite of continued treatment, and the exudate was found to contain acid-fast bacilli. Streptomycin was discontinued at the end of five months, after a total of 600 Gm. had been given, when it appeared obvious that it was accomplishing nothing.

The two other patients treated by medical means each received two Gm. of streptomycin daily by the intramuscular route, supplemented by numerous instillations of one Gm. or more of streptomycin solution into the pleural cavity after aspiration of the fluid. Each of the patients had tuberculous empyema and a bronchopleural fistula secondary to moderately advanced pulmonary tuberculosis. At the end of 120 days of treatment there was no clinical improvement in either case and roentgenograms revealed that the parenchymal lesions had not been favorably influenced.

Two of the six patients treated by surgical measures had been submitted to closed tube drainage. Each received 87 Gm. of streptomycin by the parenteral and pleural routes over a period of 55 days. The first patient was not only unimproved, but was actually worse at the end of the therapeutic trial. The second, whose tube was removed, showed no improvement until penicillin was combined with the streptomycin solution which was instilled intrapleurally after straphylococci had been isolated from the exudate. After 15 days of the combined treatment all thoracenteses were dry.

In four cases of tuberculous empyema streptomycin was used as an adjuvant to extensive surgery, as follows:

Case 9.—A 38-year-old negro man with moderately advanced tuberculosis of the right lung developed a mixed tuberculous empyema of the right pleural cavity. Examinations of the sputum were consistently negative for acid-fast bacilli but cultures from the empyema cavity were positive on several occasions, and were also positive for hemolytic *Staphylococcus aureus*. After the cavity had been unroofed and exteriorized, roentgenograms showed another large pocket in the right hemothorax; the parietal pleura was greatly thickened and the right lung was compressed to about a quarter of its normal volume. Penicillin by the parenteral route and azochloramid used locally were not effective, but over the next four months, under the influence of bed rest and supportive therapy, the temperature gradually fell to 99° F. Thoracoplasty, followed by two revisions, failed to eradicate the infection and close the cavity.

Two months later, when the patient began to expectorate rather large amounts of frothy sputum, repeated examinations of the sputum were still negative for acid-fast bacilli. Streptomycin therapy was instituted at this time, and 2 Gm. were given daily for 185 days. The patient's cough decreased and became less productive, drainage from the empyema stoma became negligible, his general condition showed progressive improvement, he began to gain weight, and the residual fistula eventually closed. The final roentgenogram showed the left lung clear, while on the right there was complete compression of the entire lung field, with no evidence of any empyema space.

Case 10.—A 31-year-old man with far advanced chronic active pulmonary tuberculosis of the upper left lobe, associated with cavitation and left tuberculous empyema, was submitted to thoracoplasty in March, 1943. He was readmitted to the hospital in 1946 because of residual cavitation in the left upper lobe, under the thoracoplasty. Lobectomy

had been contemplated, and in preparation for the operation streptomycin was given parenterally in a dosage of 2 Gm. daily for 98 days, but six weeks after antibiotic therapy was begun the empyema cavity was merely unroofed and a revision thoracoplasty was carried out. Cultures were negative for pyogenic organisms but positive for acid-fast bacilli.

Repeated aspirations of the empyema cavity were done after operation. The fluid gradually decreased in amount and became thinner, and the space was dry within about 6 weeks. Roentgenograms showed satisfactory collapse of the cavity. The patient was now symptom-free and there was no evidence of a spread of the disease to the unaffected lung.

Case 11.—A 38-year-old man with chronic active pulmonary tuberculosis of the right upper lobe was admitted to the hospital with a mixed right tuberculous empyema a month after a second-stage thoracoplasty. Culture of the exudate yielded hemolytic Staphylococcus and acid-fast bacilli. Aspirations every two days combined with penicillin replacement therapy produced no results, and it was decided that another stage thoracoplasty would be necessary to collapse the empyema cavity. This was done after streptomycin had been given intramuscularly in 2 Gm. doses for 115 days. After operation the empyema space was aspirated 3 times weekly, from 50 to 100 ml. of fluid being withdrawn each time. An anterior fourth stage thoracoplasty was performed 17 days after the third stage. The wound healed per primam. Aspirations of the cavity returned dry on the 39th day after operation. Repeated sputum examinations were negative for acid-fast bacilli, and there was no apparent spread of the tuberculous lesion to the intact lung.

Case 12.—A 30-year-old man was admitted to the hospital with numerous draining pleurocutaneous tuberculous sinuses. Thoracotomy had been necessary for a penetrating wound of the right chest and tuberculosis was later found to be responsible for the persistent drainage, which had not been checked by several revisions of the thoracotomy and by decortication. Although unroofing of the cavity resulted in a decrease in its size, the sinuses remained open. Streptomycin was then given daily for 60 days in 2 Gm. doses. After 5 weeks of therapy the sinuses closed completely and remained closed when the antibiotic was withdrawn 25 days later.

COMMENT

The three cases of tuberculous empyema treated only by medical measures make clear that streptomycin is not of value in chronic productive tuberculosis. They also make clear that bronchopleural fistulas and empyema of tuberculous origin will not improve under this form of treatment if parenchymal lesions remain unimproved. In one of the cases treated by closed tube drainage the patient became worse under streptomycin therapy, but the other, similarly treated case illustrates the advantages of combined therapy, which were also apparent in the case of nontuberculous empyema treated by both penicillin and streptomycin (Case 2).

In the first of the four cases in which streptomycin was used as an adjuvant to extensive surgery (Case 9) the closure of the residual fistula could be attributed not only to the consequence of compression of the parenchymal lesion but also to the direct bacteriostatic action of the drug on the offending bacteria. In the second case (Case 10), in which the empyema was of purely tuberculous origin, it would seem that streptomycin was of value in changing the character and consistency of the exudate, thus permitting a rapid obliteration by the surgery employed to bring about collapse. In the third case (Case 11) streptomycin made possible the treatment of a mixed empyema as a purely tuberculous empyema; good results were obtained by aspirations and surgical collapse. In this case streptomycin was administered only by the

intramuscular route. In the fourth case in this group (Case 12) streptomycin was also administered only parenterally, but its effect on the underlying focus was apparently such that residual fistulas were obliterated.

The series, small as it is, permits a preliminary definition of the uses of streptomycin in pulmonary tuberculosis complicated by empyema: 1. Streptomycin by the intramuscular or the intrapleural route or both may suppress the pyogenic organisms in a mixed tuberculous empyema and permit the case to be managed as if it were a purely tuberculous empyema. It may be advantageous, however, to add penicillin to the therapeutic regimen, to obtain an immediate, maximal suppression of the secondary invaders. 2. The bacteriostatic effect of streptomycin in an open mixed tuberculous empyema affords protection during extensive plastic maneuvers. 3. The use of streptomycin apparently is bringing about an extension of the scope of surgery in mixed tuberculous empyema by permitting a direct attack upon the visceral fibroplastic membrane. 4. The drug is of no apparent value in the parenchymal lesion of chronic productive tuberculosis complicated by empyema.

The subject has been adequately discussed elsewhere[7, 8, 9] and need not be elaborated here, but it should be emphasized again that caution must be exercised in the employment of streptomycin over prolonged periods, because of possible untoward effects, particularly on the eighth cranial nerve.

SUMMARY

Experiences in U. S. Army hospitals with streptomycin as part of the therapeutic regimen in lung abscess, nontuberculous empyema, and tuberculous empyema have been presented. The series of 17 cases is too small to permit conclusions, but certain of the results are sufficiently encouraging to warrant continued use of this method on the proper indications.

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MEMOIR

ENRIQUE FINOCHIETTO, M.D.

(1881-1948)

It is with sincere regret that the ANNALS OF SURGERY announces the death of Dr. Enrique Finochietto on February 17, 1948. His passing, in his sixty-eighth year, represents an irretrievable loss to the medical profession not only because a brilliant and inquiring mind has been silenced forever but also because the technical investigations which he and his brother, Ricardo, were

Dr. Enrique Finochietto

conducting at the time of his death have been left unfinished; these encyclopedic studies, which were eventually to be published in 16 volumes, represented years of untiring research.

Born on March 13, 1881, in Buenos Aires, Dr. Finochietto received his medical degree from the School of Medicine of the University of Buenos Aires in 1904. In 1906 he was appointed to the staff of the Rawson Hospital, in whose corridors his was a familiar figure during the remainder of his life. His gradu-

ate medical training took him not only to Europe but also to the United States, where he worked with Erdman and Harvey Cushing.

For his service *ad honorem* at the Argentine Hospital in Paris during World War I he received the Legion d'Honneur. Elected president of the College of Surgeons of the City of Buenos Aires in 1922, he also officiated as president of the Fifth Argentine Congress of Surgery. He was a member of the Academies of Surgery or Medicine of Argentina, Madrid, Bolonia, Montevideo, Paris, Rio de Janeiro, and La Pas, Bolivia.

Although Dr. Finochietto attained international recognition as a teacher, surgeon, and inventor, he remained modest and retiring. The numerous surgical instruments and appliances which he invented found universal application. His didactic methods were applauded all over the world. Ever conscious of the weighty responsibility of his profession he would frequently quote Faure:

> We live under the most extraordinary emotional circumstances. Life or death depends on us every day. A hint, a passing inspiration during a difficult operation, a gesture, a furtive look, might mean life or death. We all have this same conviction but nevertheless we never retreat before such a terrific responsibility.

He unselfishly devoted his life to the good of mankind, with complete disregard for material benefits. Only recently he financed the complete re-equipping of his operating theater at Rawson Hospital. Probably the greatest tribute which could be paid to his technical surgical skill was paid by Lord Moynihan, president of the Royal College of Surgeons, who said, after witnessing Dr. Finochietto perform an operation, "If ever I have to be submitted to the knife, let it be by this extraordinary surgeon called Enrique Finochietto."

Scientist, inventor, preceptor, surgeon, and indefatigable worker, he has left to mankind a memory of service which will be difficult to duplicate but which will serve as an inspiration to all who follow him.

—MICHAEL E. DEBAKEY.

EDITORIAL ADDRESS

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